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ECZEMATOUS AND PIGMENTARY LICHENOID DERMATITIS

Atypical Lichen Planus; Preliminary Report

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SEVERAL surprises greeted the military dermatologist when he first saw and tried to treat patients with "infectious eczematoid dermatitis" from the Southwest Pacific Area. The eruption was resistant; even mild eczematous lesions were characterized by exacerbations; purplish to almost coal black splotches of hyperpigmentation were common; exfoliative dermatitis was not uncommon; severe unexpected complications were not rare; follicular hyperkeratoses were the rule and one group of patients had a disease which closely simulated lichen planus with lesions of the mucous membrane and skin. It seemed entirely likely that in all the cases there was a common denominator. It is my desire to describe the various manifestations of the disease, to record my observations in over 300 cases and to comment on its causation.

This disease, protean in its manifestations, was at first thought to arise only in the New Guinea Area. Cases have now been observed also from the Mediterranean Theater, and although the number is small the clinical characteristics are identical.

TYPES

On the basis of clinical features, the eruptions can be divided into the dry type, comprising approximately 20 per cent of the cases from the Southwest Pacific, and the exudative type, comprising 80 per cent. Too few cases from the European Theater have been observed by me to permit a determination. Either type may be mild or severe, and both may present complications. Both types may be present in the same person and at the same time. In some cases the lesions first are dry and then become eczematous and again are dry when the patients arrive at the general hospitals in the Zone of the Interior. Dry lesions usually become eczematous if overtreated. Among recent evacués from the Southwest Pacific Area there is an increasing percentage of eczematous eruptions and the eruptions are much less severe. This is probably due to

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earlier hospitalization, fewer attempts to return the soldier to duty and earlier evacuation. Many of the patients with severe eruptions received earlier had been given five or six trials at duty between hospitalizations. Many of the earlier patients with eczematous lesions after improving in the hospital were given furloughs in Australia, where the eruptions of a large percentage improved greatly or cleared entirely. On their return to New Guinea, a large number had recurrences before they could rejoin their units. In many patients, oozing disappeared within three or four days after they had left the tropics.

Dry Type.—Dry lesions frequently begin as indefinitely outlined, pruritic, erythematous, slightly scaling eruptions of the webs of the fingers, on the medial surfaces of the thighs, the palms and soles, the dorsa of hands or feet and occasionally on the face. When first observed in this country, the skin in most cases presents mild to severe dryness, usually of the extremities, with discrete and grouped keratotic follicular papules. Many of the papules present central hyperpigmentation. Many present also indefinitely outlined splotches of pigment about and between the clustered papules. In cases of the more advanced disease there may be present a generalized eruption of the same type, except severer with coalescence of the follicular elements within the patches and increased hyperkeratosis forming variously sized nodules (the largest I have seen were the size of a large hazelnut), covered with a dirty gray, tightly adherent scale. These nodules resemble rather closely the lesions of hypertrophic lichen planus; they often have a deep purple cast and are sometimes angular. I, however, have never seen the phrynoderma of the new disease in conjunction with true lichen planus. In the new disease I have never seen the "cobweb" network so typical of a lichen planus papule. However, a peculiar network is often observed in the atrophic scarlike residuals of healed lesions (fig. 1).

A number of patients present lesions of the mucous membrane which are clinically indistinguishable from classic lichen planus with discrete and confluent, milk white macules and papules, bars, circles and segments of circles and plaques. Some of the plaques, especially on the tongue, are intensely painful, decidedly hypertrophic, angular in outline, sharply marginated and immediately surrounded by a deep, bright red fissure which bleeds easily.

Nodules resembling those of folliculitis decalvans but with more inflammatory reaction, more hyperkeratosis and less atrophy frequently occur on the scalp and result in alopecia. No patient with alopecia was under my observation for more than four months, and growth of hair had begun again in all but 2. In several the growth was scanty and devoid of pigment.

Some lesions present even more coalescence, resulting in large indefinitely outlined thick plaques covering the dorsa of the hands, dorsa of the feet, shins, legs, buttocks and arms (fig. 2).

The nodular lesions slowly clear, with or without treatment, and I cannot state that any local treatment is of value. It was not unusual to see all lesions completely flatten, except one or two, which looked much like soft fibrous nevi but with more pigment. These lesions were

Fig. 1.—Blond soldier from Mediterranean Area in whom extensive grouped follicular hyperkeratoses developed but did not progress to nodule formation except on hands.

believed closely akin to infectious granulomas and were removed surgically or by electrodesiccation.

Secondary atrophy was common at the site of former nodular lesions on the face, body, arms and legs, where it resembled but did not duplicate that described in lichen planus of the sclerotic-atrophic type. These lesions were not ivory white but contained much pigment (fig. 1). On

the dorsa of the hands, dorsa of the feet and legs, where the preceding dermatitis was of the thick plaque type, the atrophic patches were parchment-like with violaceous discoloration but the small venules could not be visualized as in acrodermatitis chronica atrophicans, and in none was the atrophy so complete (fig. 3).

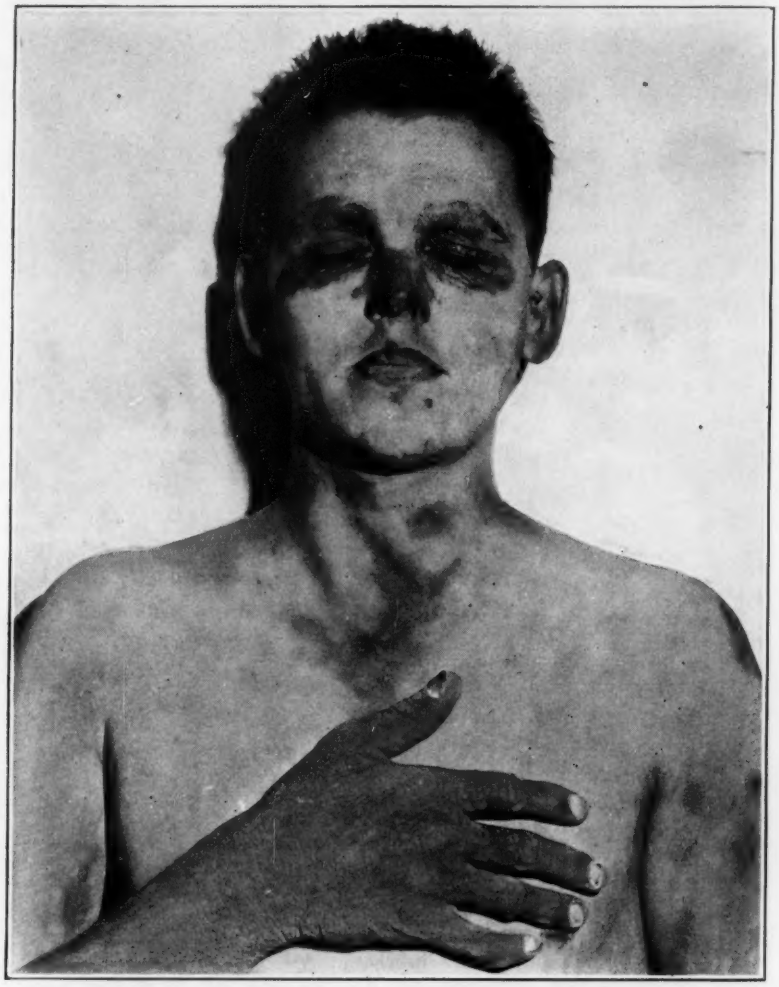

Fig. 2.—Patient from New Guinea Area with almost coal black hyperpigmentation of eyelids, nose, ears, neck and arms. Also, note extreme hyperkeratotic changes on dorsa of hands, covered with "dry cement" scaling.

The nails in the cases of severest eruptions of both types, especially the dry type, were thickened, dirty gray, friable and eroded. In some cases the nails had been lost. Paronychia was not common. No treatment was of value. As the dermatitis improved, the new growth of nail

became more normal, and patients observed over a long period finally had nails which were relatively normal.

Pigment.—Observations regarding pigment in these cases are of interest. All patients admitted to this hospital had varying degrees of yellow discoloration so typical in patients ingesting quinacrine hydrochloride (atabrine); there was no parallel between the intensity of this

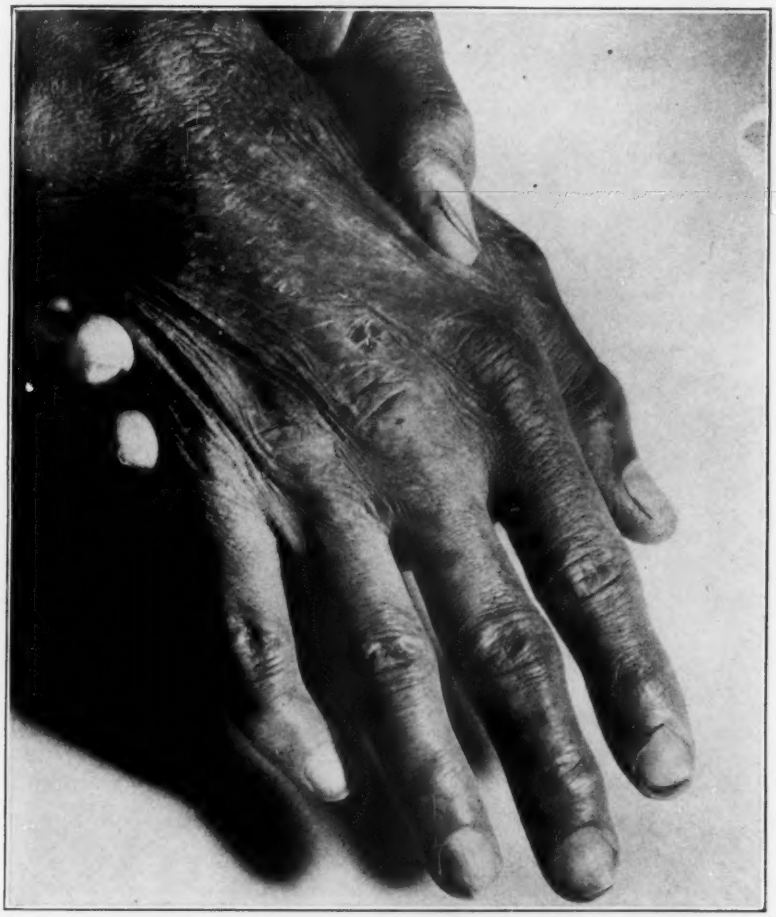

Fig. 3.—Atrophy and hyperpigmentation of the skin following resolution of hyperkeratotic dermatitis. Same patient as in figure 2, three months later.

pigmentation and the darker patchy pigmentation. The yellow pigment was, as a rule, lessened or absent in sites where former superficial lesions had resolved. The dark pigmentation occurred in variously sized and shaped, indefinitely outlined patches, tending to oval configuration, with the long axis of the lesions parallel to the cleavage lines of the skin, especially on the lids, neck and chest. The color varied from purplish

slate to purplish brown to almost coal black. Splotches of dark pigment were common on the ears, around the eyes, on the lips, nose, neck and abdomen, in the axillas and groins, not infrequently on the gums and occasionally on the hard palate and the nail beds. Pigmented areas frequently were not at the site of earlier erythema or dermatitis, and

Fig. 4.—Generalized symmetric eruption, same patient as in figure 2, showing hyperkeratosis and extreme melanin pigmentation of neck and shoulders.

dermatitis did not always develop at the site of the pigmentation. In 2 cases the ears were almost coal black; 1 of these was contracted in New Guinea and 1 in Italy. In both, the pigmentation definitely diminished during the period of observation but it was still decided when last observed (fig. 4).

It was believed that all hyperpigmentation would eventually disappear. No treatment, except time, was of value.

The following observation was of interest: One medical officer had extensive vitiligo of both lower lids, dorsa of the hands, scrotum, feet and legs prior to entrance on active duty. While in Hawaii, with prolonged exposure to the sún, he had no eruption except slight erythema with some pruritus on the dorsa of the hands and the expected "tanning" of his normal skin. Within one week after his arrival in New Guinea, after he had taken quinacrine hydrochloride en route, a severe pruritis with

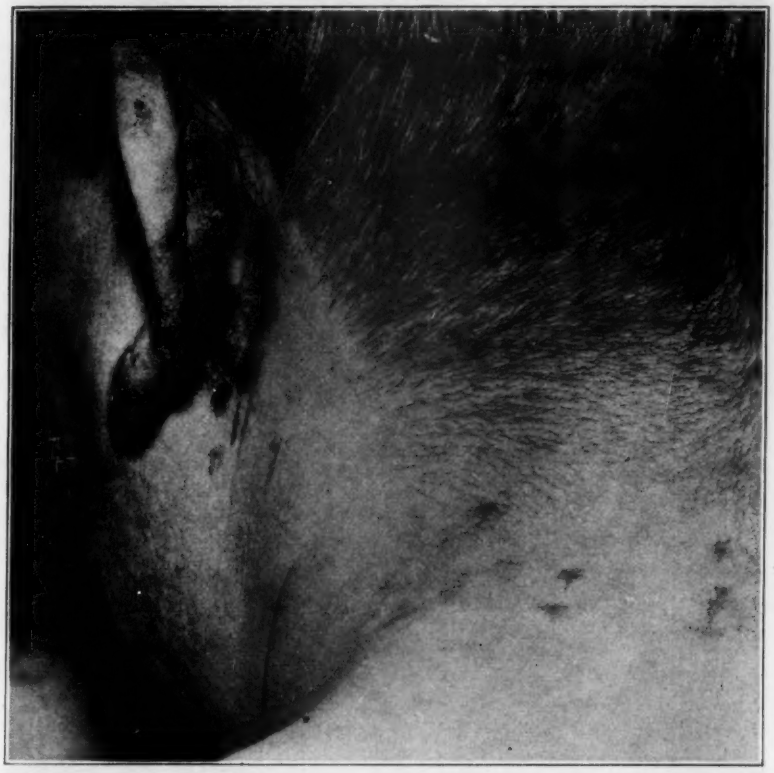

Fig. 5.—Patient from Mediterranean Theater, showing hyperpigmentation and eczematization in same area. Note pigmented macules on neck.

some papular elements developed on the dorsa of his hands following exposure to sunlight. He then wore gloves, and one week later a pruritic erythematopapular eruption developed on his shins which had not been exposed to the sun in New Guinea. A few days later other portions of the body became involved, and he noted patches of purplish black pigmentation in the tanned areas on the face, ears, lips, neck, arms and legs. When he came under observation at this hospital two months later, he presented an erythematopapulonodular eruption which involved

the yellow-tinted skin and the vitiliginous skin to about the same degree. The eruption of the vitiliginous skin was brightly erythematous only, while that of the normally pigmented skin presented also purplish brown pigmentation. It was concluded that the pigment originated

Fig. 6.—Hyperpigmentation and eczematization in the same region, patient from New Guinea. Note resolving hyperpigmented lesions on chest and in axilla.

locally in the skin and was due to some unknown factor, probably of hematogenous origin, which stimulated the normal pigment-forming mechanism. This factor was not sunlight, because the legs had not

been exposed to sunlight in New Guinea. Because this pigment takes the Becker stain, which is considered specific for melanin, the pigment is undoubtedly melanin.

Exudative Type.—The exudative type more often began as an indefinitely outlined pruritic, erythematovesicular, patchy eruption on the fingers, on the dorsa of the hands or feet or in intertriginous areas. Not a few were diagnosed by the first medical officers to see them as dermatitis venenata, dermatophytosis or tinea cruris. The vesicles soon ruptured and became infected. Rapid extension of the eruption took place in some, while in others it remained relatively stationary for a time, only to "explode" suddenly and become generalized or even universal within a few days. Exudation was usually patchy but was often generalized. Many patients with eczematous lesions exhibited also patches of hyperpigmentation in the same areas (figs. 5 and 6).

Crusts may be few or many and often cover pus-exuding lesions. In several cases of long-standing eruptions vegetating lesions developed.

Several patients with eczematous lesions only had lichen-planus-like lesions of the oral mucous membrane. In approximately 6 per cent of my cases there developed generalized to universal exudative dermatitis with profuse exfoliation (fig. 7).

FACTORS IN ETIOLOGY

It is impossible at the present time to evaluate a number of observations. I have observed the disease in 1 Japanese, several Indians and approximately 300 white persons of various nationalities and ancestry but in no Negroes. Both types have been observed in blonds and brunets. The nodular type was relatively more common in blonds.

Dermatologists have long observed that exudative eczema, impetigo and infectious eczematoid dermatitis tend to become exacerbated and that contact dermatitis from either plants or drugs is more likely to develop on hot humid days. Appetite lessens, and loss of weight is the rule during hot summer months. All but a few cases of this disease to date have come from the New Guinea region which lies between 10 S and 10 N latitude. Temperatures at sea level seldom rise above 95 F. and rarely fall below 70 F. The average relative humidity at five coastal stations throughout the territory over a five year period is 81 per cent at 9 a.m., 75 per cent at 8 p.m. and 88 per cent at 9 p.m.[1] Most patients stated that after a few weeks they "lost their appetite" and often discarded part of their food. Most of them had lost 10 to 50 pounds (4.5 to 22 Kg.) in weight, although a few had not. Recent evacués lost less weight than those returned several months ago.

There is no relation of the disease to combat, and some of the severest eruptions occurred in Service Force troops at fixed bases.

1. Challis, B. G.: Climatic Notes on New Guinea, New Guinea Agric. Gaz., December 1939.

Hygiene is probably a factor in determining the rapidity with which infection develops.

It has been repeatedly observed that the skins of these patients are easily infected and are easily irritated by medicaments which the skins of patients in the midwest section of the United States usually

Fig. 7.—Exudative exfoliation in a case of universal dermatitis. Patient had typical hyperpigmented nodular lesions on the chest. He was an American-Italian soldier from New Guinea.

tolerate well. Many eruptions promptly become exudative when the weather becomes hot and humid for even a few hours. It must be concluded that something has happened to these skins which renders them more vulnerable to both infection and irritation.

Several authors have described phrynoderma and hyperpigmentation with lichenification following the ingestion of diets deficient in vitamin A with improvement following large doses of that vitamin over long periods. In many of the cases cited here the patients were on C and K rations but did not eat all the ration. A complete C ration contains 9,450 U.S.P. units of vitamin A, and K ration contains 4,674 U.S.P. units. The minimum daily requirement of a 70 kilogram man on moderate activity is 3,000 U.S.P. units, and the recommended daily allowance is 5,000 units.[2] As far as I know, the requirement for persons at hard labor in a hot humid climate has not been determined. Vitamin A is known to be unstable, especially at high temperature. It is usually conceded that there is wide variation in the ability of different persons to utilize vitamin A, although most writers believe that huge amounts of the vitamin can be stored in the body provided there is adequate intake. The ability to absorb vitamin A is greatly diminished when diarrhea is present, and many soldiers in the New Guinea Area had diarrhea from various causes. Some authors contend that the entirely adequate diet should contain a safety factor of 100 per cent.[2] It is readily understood that much more investigation is necessary before definite statements can be made regarding the role of vitamin A as a predisposing factor in the disease discussed in this paper.

Most of the patients from both theaters had no fresh milk and little fresh fruits or vegetables for prolonged periods. On the other hand, many patients were given supplemental vitamins, especially vitamin A, some in large doses, without benefit. In this regard, it is recalled that McCollum in 1917 pointed out that in rats on diets deficient in vitamin A there developed severe spontaneous infections of the skin. However, this has not been proved to apply to man.

Almost all the patients in this series had mild to severe anemia. The whole problem of the porphyrins with regard to this disease needs investigation and promises to be worth while. Cultures have been negative for bacteria and virus. Few bacteria have been demonstrated in the biopsy sections and then only in the epidermis.

Insecticides are being studied by some investigators as the cause of certain cases of aplastic anemia and polyneuritis. While all the patients in this series had been exposed to insecticides, I currently believe that these materials play little or no part in producing the disease described in this paper.

Observations regarding quinacrine hydrochloride will be discussed later.

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2. Food and Drugs, Federal Register (No. 227) **6**:5922-5925 (Nov. 22) 1941, title 21; cited in Inadequate Diets and Nutritional Deficiencies in the United States, Bulletin 109, National Research Council, Washington, D. C., November 1943, p. 3.

PATHOLOGY

In addition to the anemia, most patients also have an elevation of circulating eosinophils from 3 to 35 per cent. Sections of tissue usually contain an increased number of eosinophils.

The microscopic picture varies, depending on whether the eruption is "dry" or "exudative." The most decided changes are found in the dry type, which presents mild to severe hyperkeratosis and varying degrees of acanthosis. Some lesions exhibit decided pseudoepitheliomatous hyperplasia (fig. 8 *A*). The hyperkeratosis tends to involve the entire length of the hair follicle and is often surrounded by perifollicular cellular infiltrate (fig. 8 *B*). Some spongiosis is present in the basal cell and prickle cell layers. Clear cells are common in the malpighian layer, and in some areas the basal cell membrane is indistinct (fig. 9 *A*). An increase of melanin in the basal cell layer is a constant feature and is patchy in type, varying from mild to intense and not always at the site of the underlying infiltrate. Dendritic cells and basal cells are often loaded with pigment (figs. 9*B* and 10*A*), some of which may continue outward through the stratum corneum (figs. 9*B* and 10*A*). The basal cell layer in some areas shows little increase of pigment, which seems to have "shaken out" and appears in clumps in chromatophores in the cutis where it tends to immobilize, especially in the tips of the papillae (figs. 9*B* and 10*A*). Pigmentation is less intense in areas where acanthosis and pseudoepitheliomatous hyperplasia are more evident (fig. 8*A*). Some sections present a classic picture of "lichen planus" (fig. 10*B*). All sections demonstrate atrophy to absence of sebaceous glands, although the erector muscles are often retained. Atrophy of the hair follicle is demonstrated in some cases. Sweat glands may be unaffected or surrounded by infiltrate, and some atrophy may occur. Secondary eczematous changes may be present in varying degrees, with eosinophilic infiltrate, but even in these cases the hyperkeratosis and the atrophy of the sebaceous glands are retained. The end stage is characterized by increased pigmentation, thinning of the rete ridges and atrophy of the dermal appendages. I believe that some of the atrophic appendages later regenerate. No attempt was made to prove this contention by second biopsies, and the belief is based on clinical observation alone.

CLINICAL COURSE

Some observers in the New Guinea Area and I have seen numerous complications, including universal exfoliative dermatitis, hepatitis, atypical pneumonia, polyneuritis, heart bundle-branch block, pericarditis, ascites, a low level of total protein in the blood, reversal of the albumin-globulin ratio, edema and anasarca, simple anemia and aplastic anemia. In 2 patients of this series there developed pulmonary tuberculosis.

Simple anemia is common in both types of the disease. Exfoliative dermatitis was observed in both types. Atypical pneumonia occurred in 2 patients with exudative eruptions at this hospital. I have

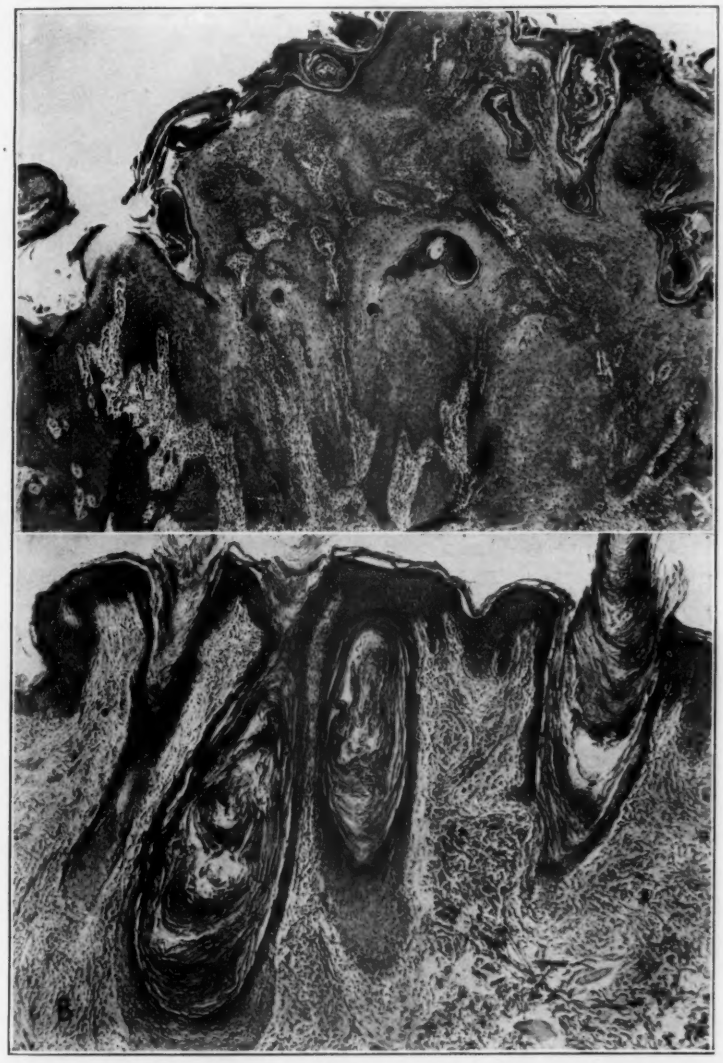

Fig. 8.—*A*, biopsy specimen showing verrucous lesion with decided acanthosis and pseudoepitheliomatous hyperplasia. Hematoxylin and eosin. × 30. *B*, keratotic plugging of follicles and perifollicular hyperplasia greatest at depth of follicles but with some atrophy of follicular walls. Hematoxylin and eosin. × 48.

observed 4 patients with paresthesia of the extremities, 2 of whom exhibited muscular incoordination in all four extremities. All 4 had an increased amount of globulin in the spinal fluid and an elevated

level of total protein, between 105 and 175 mg. per hundred cubic centimeters, without other changes. The eruptions of all 4 were "dry." Several patients with aplastic anemia in conjunction with this dermatosis were observed in the Southwest Pacific Area, and 2, of whom 1 died,

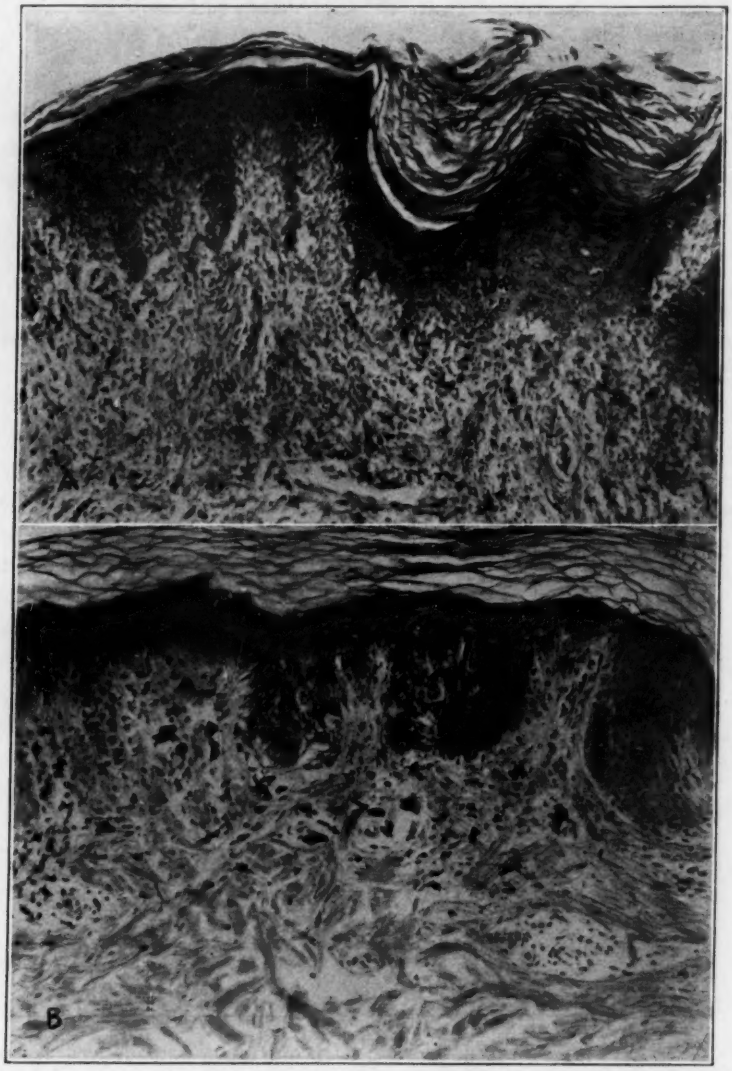

Fig. 9.—*A*, hyperkeratosis, thickening of granular cell and prickle cell layers, narrowing of rete pegs, some liquefaction of basal cell layer and intense cellular exudate in papillary and subpapillary layers consisting principally of histiocytes and lymphocytes. Hematoxylin and eosin. × 85. *B*, acanthotic process with increase in granular layer. Numerous dendritic cells laden with melanin pigment and pigment-laden chromatophores in the cutis. Silver nitrate and hematoxylin. × 155.

have been seen at this hospital. In both the eruptions were of the "dry" type. Heart bundle-branch block was observed in 2 patients with dry dermatitis. Ascites occurred in 2, the eruption of the one being dry and of the other exudative. Low levels of total protein in the blood

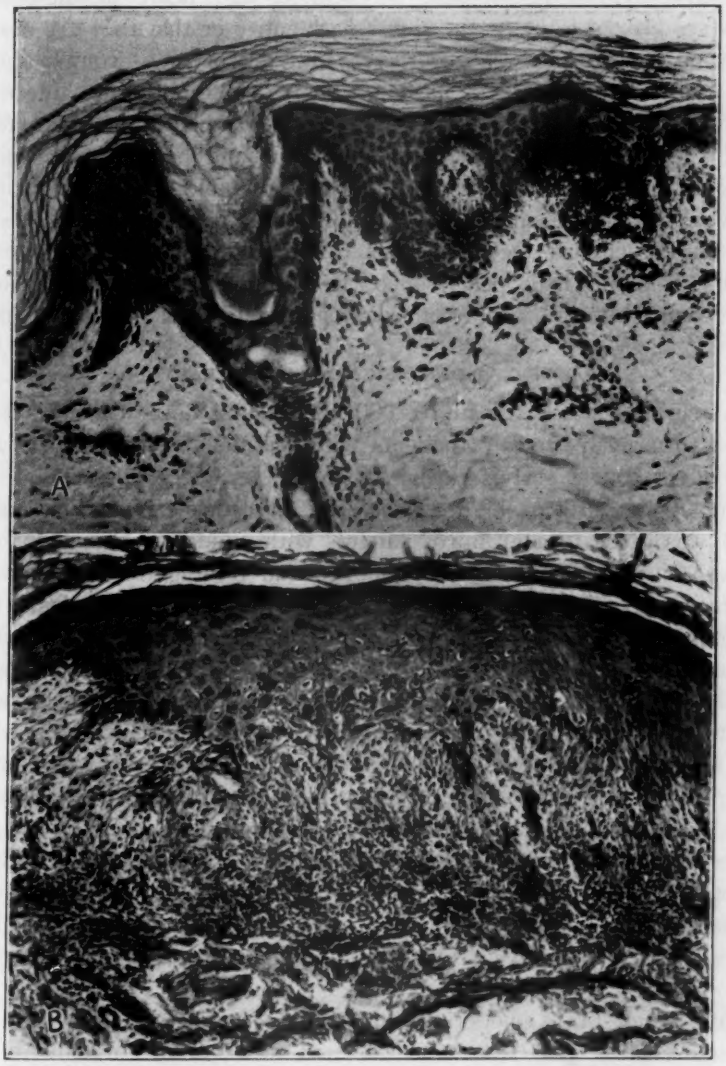

Fig. 10.—*A*, section from patient with disease resembling Riehl's melanosis showing keratotic plugging of sweat duct and tremendous increase in pigment in small area involving basal, dendritic and clear cells and extending up into stratum corneum and down into chromatophores in the cutis. Silver nitrate and hematoxylin. × 115. *B*, typical picture of "lichen planus" with hyperkeratosis, increase in granular layer, liquefaction degeneration in basal cell layer and cellular infiltrate limited to upper portion of cutis. Section also showed atrophy of hair follicles, dilatation of sweat glands and definite increase in melanin pigment. Hematoxylin and eosin. × 85.

are common in patients with severe exudative eruptions, while a reversal of the albumin-globulin ratio with edema was observed in 4 and anasarca in 1.

I do not desire to give the impression that all these conditions, especially atypical pneumonia, polyneuritis and heart bundle-branch block are proved to be due to the disease entity or that they are due to the same etiologic factors. However, they did occur as complications. Major Clarence Livingood has seen numerous diphtheritic infections secondary to the disease under discussion, especially the eczematous type, and has encountered both polyneuritis and heart bundle-branch block in some of his cases. Although it is possible that the 6 patients reported on in this paper had had diphtheritic infections there was no note in the clinical record to this effect, and the patients gave no history of having had open lesions. It is, therefore, believed that both these conditions are probably unusual manifestations of the disease itself.

OBSERVATIONS REGARDING THERAPY

Vitamin A was given in 100,000 U.S.P. unit doses daily for three weeks to a small group of patients with eruptions of both types, with no evident benefit. It is realized that the period of observation was short. A high protein, high carbohydrate, low fat diet (modified Varco diet) was given to a group of patients with exudative lesions for two weeks, with no definite effect. Supplemental feedings of Dietene were given to some patients and were believed to be of some benefit in that the gain of weight was more rapid. Intramuscular injections of bismuth subsalicylate were given to several patients with nodular eruptions. No definite benefit was noted. Injections of mercurial preparations were not tried. One observer overseas noted generalized exudative dermatitis following intravenous administration of oxophenarsine hydrochloride (mapharsen). I gave solution of potassium arsenite U.S.P., in ascending doses, beginning with 2 minims (0.12 cc.) three times a day and increasing by 1 minim (0.06 cc.) a day, to 4 patients with nodular eruptions, with 100 per cent poor results, manifested within two weeks by increased pruritus, oozing dermatitis, edema of the lower extremities and albumin, red blood cells and granular casts in the urine. The drug was promptly discontinued.

Mild and severe pyoderma universally responded well to penicillin intramuscularly in 20,000 to 50,000 unit doses every three hours for a total of 200,000 to 1,000,000 units. Local applications of penicillin in wet dressings seldom controlled the infection and frequently produced dermatitis when used in concentration of 250 units per cubic centimeter. Five per cent sulfadiazine ointment occasionally gave good results in cases of mild and localized eruptions but frequently produced exacerbations.

Wet packs of solution of boric acid constantly for three to ten days in the cases of acute eczematous eruptions was the most satisfactory, although several failures were noted. Some of these failures responded to solution of potassium permanganate (1 : 10,000) applied in wet dressings and some to 0.12 per cent silver nitrate solution packs. Solution of aluminum acetate and alibour water (water containing zinc and copper sulfates) in proper dilutions gave satisfactory results in a few cases but often failed. Few patients in my experience tolerated boric acid ointment, for some reason yet unknown. Twenty per cent zinc oxide in Aquaphor (an oxycholesterol-petrolatum ointment base) was usually well tolerated after boric acid packs were discontinued. Three to 5 per cent ammoniated mercury in Aquaphor base was helpful in some cases.

For eczematous eruptions with vegetating lesions and for those with infiltrated pyogenic lesions roentgen irradiation in doses of 100 r weekly for four or five weeks proved most beneficial. Chronic exudative patches also usually responded after one to four irradiations.

Blood plasma and concentrated human serum albumin daily proved helpful in cases of extensive eczematous eruptions with low total protein in the blood and especially in those with reversal of the albumin-globulin ratio. It is desired to caution against the use of plasma in cases in which it is not needed because of the possibility of plasma or infectious hepatitis and jaundice three or four months later.

Relation to Malaria and Quinine.—Some of the patients had malaria overseas and in this hospital. Some had their first attack in the hospital. A few had no malaria. In 1 patient aplastic anemia developed two weeks after treatment of an attack of malaria with quinacrine hydrochloride. During the period of anemia, the patient had several slight chills with fever, but blood smears were consistently negative for plasmodia. After several transfusions, a sternal puncture was done. Many malarial parasites were demonstrated in the marrow smear. After this observation, several patients without known malaria were given quinine as in the treatment of malaria, and the dermatitis was not affected.

Quinacrine Hydrochloride and Dermatitis.—Several patients had two to four attacks of malaria in this hospital. The first attacks were treated with quinacrine hydrochloride. In none of the cases did the dermatitis improve during the period of treatment. Three patients with dry lesions and involvement of the mucous membrane manifested increased soreness of the tongue and increased prominence of the lesions. In 1 patient with dry lesions severe exfoliative dermatitis developed on the fourth day of treatment. In several there developed increased pruritus with slight oozing in the groins. Several eczematous eruptions became

more exudative. Subsequent attacks were treated with quinine. A few patients manifested slight exacerbations of the dermatitis with the second attack of malaria which was treated with quinine. None had exacerbations with subsequent attacks which were treated with quinine, and several actually improved during the period of treatment. Three patients with previous exacerbations of their lesions during an attack of malaria treated with quinacrine hydrochloride were then given quinacrine as in the treatment schedule. There were exacerbations of the lesions of 2 in two days and of those of 1 in four. Two patients with patchy eczematous lesions, which had been dry for two and three weeks, respectively, and who had been receiving suppressive therapy with quinine, were given 0.65 Gm. of quinacrine hydrochloride daily. In the one increased pruritus and oozing developed on the fourth day and in the other on the ninth.

It is worthy of note that not all the eczematous eruptions became aggravated when the drug was being taken. Patients with dry nodular lesions almost universally noted increased pruritus, increased infiltration and more elevation of the nodules after taking daily doses of 0.3 or 0.65 Gm. of the drug for two to four weeks and some in much less time.

Quinacrine Hydrochloride and Quinine as Suppressive Agents.—Observations at this hospital agreed with those at others in that quinacrine hydrochloride proved a more efficient suppressive agent than quinine.

Patch Tests.—Test patches with quinacrine hydrochloride being used in Aquaphor base in dilutions of 1:1,000, 1:200, 1:100 and 1:10 were applied to the normal-appearing skin of 7 patients, 4 with eczematous eruptions and 3 with the dry type, as well as to 4 controls who had never taken quinacrine hydrochloride. All tests elicited negative reactions after seventy-two hours, except that of 1 patient with a generalized dry patchy follicular eruption (shown in figure 1) from the Mediterranean Area, who exhibited rather intense erythema with a moderate papulovesicular dermatitis at the site of the patch which covered a few maculopapular lesions. Aquaphor containing 1 per cent quinacrine hydrochloride was applied to small patches of skin of 3 patients with universal dermatitis which had become subacute. In all 3 acute vesicular dermatitis developed under the patch within twenty-four hours. In 2 of these there developed an exacerbation of the generalized dermatitis. Two patients with localized patches of dry dermatitis which had previously become exudative after the drug had been taken by mouth and whose normal skin did not react to test patches with 1:10 quinacrine hydrochloride ointment applied 1:100 ointment to small areas within the patches every three hours for three days. On the third day, each had a vesicular eruption in the patch where the ointment was applied. A

vesicle occurred at each follicular opening, and there was little intervesicular erythema. Other patients were then tested, and with only one exception all the tests elicited the same reaction. Eczematous lesions in soldiers who had never taken the drug did not give this reaction. It was thus concluded that only that skin on which there had previously been an eruption was reactive.

COMMENT

From the foregoing observations, I am convinced that quinacrine plays the major part in the causation of this new disease entity. Whether it is the entire cause must be left to further investigation.

The observation of one investigator overseas and of myself that arsenic, either oxophenarsine hydrochloride or solution of potassium arsenite U. S. P., produces very adverse effects is interesting. It is worthy of note that practically all the manifestations of this new disease have been observed following arsenical medication.[3] Symptoms of chronic arsenical poisoning are usually given about as Davison [4] gave them: Weakness, anorexia and jaundice may be present and often low fever; "overgrowth of horny layer, especially palms and soles. Frequently there appears an arsenic melanosis. Anemia is a common result of prolonged use of arsenic. Multiple neuritis may occur; this generally involves the limbs rather than the trunk. Paralysis of sensation followed by motor paralysis is not uncommon." Feinberg [5] wrote: "We are forced to regard these manifestations as reactions due to allergy. Among such common effects of hypersensitivity are dermatitic rashes of various types, urticarial eruptions, fixed drug eruptions, exfoliative dermatitis, hepatitis and other types of liver damage, hemorrhagic brain lesions, hematopoietic disturbances including aplastic anemia, granulocytopenia and thrombocytopenia, asthma and rhinitis and anaphylactic shock. The specificity of these reactions varies in different persons. In some it extends to practically all arsenicals, although in a larger number the benzol radical is the active part of the antigen." It is interesting that both the arsphenamines and the quinacrine hydrochloride contain benzyl radicals. The same author stated, "The status of skin tests in arsphenamine allergy is uncertain. It is true that patch reactions are often obtained, but such reactions are frequently present in those who show no clinical allergy and are often absent in those who display frank allergic symptoms." He also cited experiences of Sulzberger and Simon

3. Sulzberger, M. B.: Dermatologic Allergy, Springfield, Ill., Charles C Thomas, Publisher, 1940, p. 294.

4. Davison, F. R.: Synopsis of Materia Medica, Toxicology and Pharmacology, ed. 2, St. Louis, C. V. Mosby Company, 1944, p. 535.

5. Feinberg, S. M.: Allergy in Practice, Chicago, The Year Book Publishers, Inc., 1944, p. 343.

with sensitiveness to arsphenamine in guinea pigs, which could be sensitized in some cities but not in New York.. The effect of the climate per se on allergy is not understood.

Just how long quinacrine can be retained within the human body is not yet known, although Kehar, working with monkeys, has reported elimination prolonged up to fifty-one days and others have reported retention for as long as sixty-nine days.

One of the tests for quinacrine is its yellowish green fluorescence under ultraviolet rays in solutions up to 1 : 5,000,000 dilution. A section of liver from 1 patient in this series, who died of aplastic anemia, gave a brilliant fluorescence after one month's immersion in solution of formaldehyde. The patient had taken no quinacrine hydrochloride for two months.

SUMMARY AND CONCLUSION

A protean disease with symptoms which are mainly dermatologic but with numerous somatic manifestations, occurring with great frequency in the New Guinea Area and with much less frequency in the Mediterranean Theater, is described.

The cause is not known, although several factors are probably involved, including low vitamin intake, especially vitamin A, quinacrine hydrochloride (atabrine) and allergy. It is believed that vitamin A deficiency predisposes to the disease but that quinacrine hydrochloride is the major factor.

The symptomatology and classification are given.

The pathologic changes are described and illustrated.

The importance of this disease is expected to diminish rapidly as large concentrations of troops are moved from New Guinea and Southern Italy.

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NEURODERMATITIC REACTION

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BY NEURODERMATITIC reaction we mean a pathologic process, and not a disease. The term is used because the microscopic changes in this process are similar to those found in the disease neurodermatitis. The reaction is characteristic of such dermatoses as neurodermatitis, nummular eczema and exudative lichenoid and discoid chronic dermatosis.

It is often difficult clinically to diagnose these dermatoses and to differentiate others from them. A microscopic diagnosis would be of considerable assistance, but, unfortunately, this is not always conclusive. The subject is of sufficient importance to stimulate further study. This presentation may suggest a somewhat different point of view as a basis for new investigations.

The neurodermatitic reaction involves both the cutis and the epidermis. The latter is usually acanthotic and shows some degree of regularity; there is, as a rule, little evidence of edema. A focal infiltration composed of small round and wandering connective tissue cells is found about the vessels of the middle and the upper layer of the cutis, and the walls of the arterioles and small arteries are thickened. These findings are not constant, and the differential diagnosis depends on these variations.

We offer the following outline which includes not only the dermatoses characterized by the neurodermatitic reaction, but also indicates the diseases from which they must be differentiated.

THE NEURODERMATITIC REACTION

I. Neurodermatitis

A. Neurodermatitis disseminata

B. Neurodermatitis circumscripta (lichen chronicus simplex of Vidal)

From the Skin and Cancer Unit, New York Post-Graduate Medical School and Hospital, Columbia University, New York.

II. Nummular eczema { with edematous vesicle / with cellular vesicle

A. So-called pustular psoriasis

B. Pompholyx

1. Type due to increase and retention of sweat
2. Type due to fungous infection

C. Dermatitis venenata (contact dermatitis)

1. with edematous vesicle
2. with cellular vesicle

III. Exudative lichenoid and discoid chronic dermatosis

A. Iodide or bromide eruption

B. Lymphatic leukemia

C. Mycosis fungoides

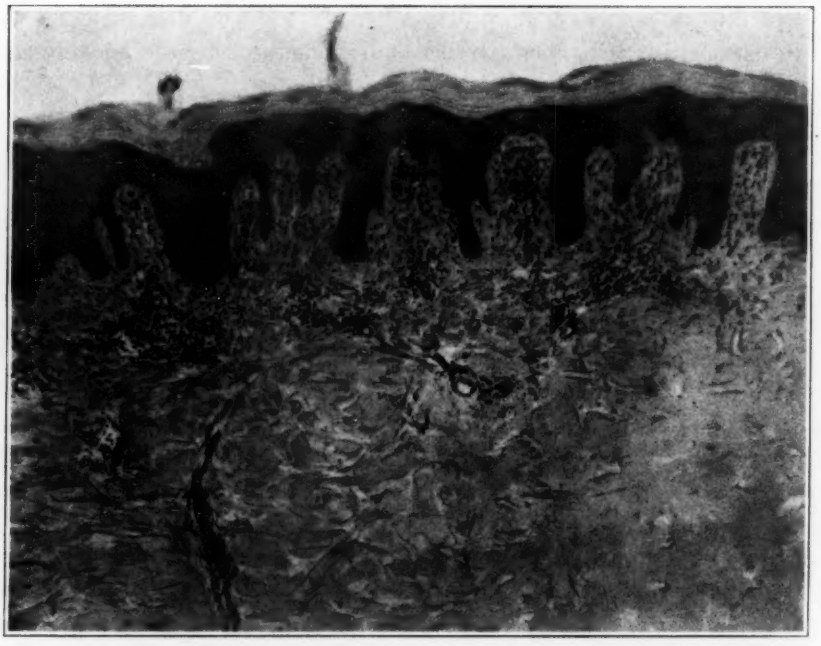

Fig. 1.—Neurodermatitis disseminata. Note regular acanthosis and focal cellular infiltration about the vessels of the middle and upper layers of the cutis. × 88.

NEURODERMATITIS

The clinical picture of neurodermatitis needs no comment. The pathologic process involves both the epidermis and the cutis: The former is dry and, although the intercellular spaces may be accentuated, the basal cell margin is unaltered; the granular and horny layers are present and may be increased, and a rather regular acanthosis is usually present. However, friction, scratching, medication, etc., may super-

impose a traumatic dermatitis. This would account for the presence of an irregular acanthosis, edema and even parakeratosis. We feel that these are evidences of secondary eczematization and not part of the disease itself.

The small vessels of the middle and upper layers of the cutis are dilated and their walls thickened. About them is a focal infiltration of small round and wandering connective tissue cells; there are no plasma, epithelioid or giant cells. Throughout the area is moderate interstitial edema; the papillary bodies are not exaggerated; the elastic tissue is unchanged, but, where the cellular infiltration is pronounced, it may be pushed aside.

There are clinical differences between lichen chronicus simplex and neurodermatitis disseminata, but both present the microscopic picture which has been described. Therefore the pathologic findings cannot establish a final diagnosis unless they take into consideration the clinical features.

NUMMULAR ECZEMA

Nummular eczema occurs in various-sized discoid or oval patches. It is found on the dorsal surface of the hands, the fingers and the forearms; it also appears on the extensor surfaces of the thighs and the legs. Although both the upper and the lower extremities may be involved, there is no symmetry. Each lesion is an inflammatory erythematous patch containing grouped vesicles. The size of these patches varies from that of a dime to that of a quarter, or larger. The vesicles persist until they finally break and form crusts. Severe itching is constantly present. The patches appear suddenly and spread peripherally; occasionally they undergo involution in the center, leaving a brownish discoloration; however, no atrophy or scarring results. In time, new lesions appear on the same, or new, locations.

Although this is the usual clinical picture, other manifestations are frequently seen. Lesions may appear anywhere, patches may be large, or smaller ones may fuse together and cover a considerable surface of the skin. Vesicles and crusts may be absent, and there may be only an erythematous, scaly area. Thus, the disease may simulate eczematized neurodermatitis, contact dermatitis, seborrheic dermatitis, dermatophytosis, dermatophytid, dermatitis herpetiformis and other varieties of eczema.

The pathologic features of nummular eczema differ from those of neurodermatitis only by the presence of an intraepidermic cavity. When the process has dried or even in a well developed lesion in which the vesicle is missed, the features are identical. However, in a typical picture this epidermic cavity is the differential feature. There may be one or more vesicles; these may be large or small and contain fluid,

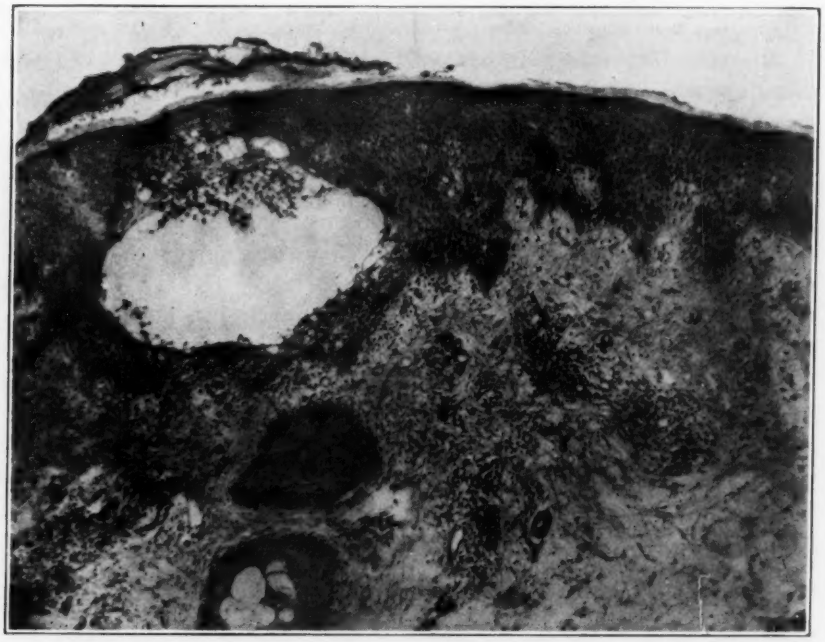

Fig. 2.—Nummular eczema. Note the edematous type of vesicle in the epidermis and focal cellular infiltration about the vessels. × 88.

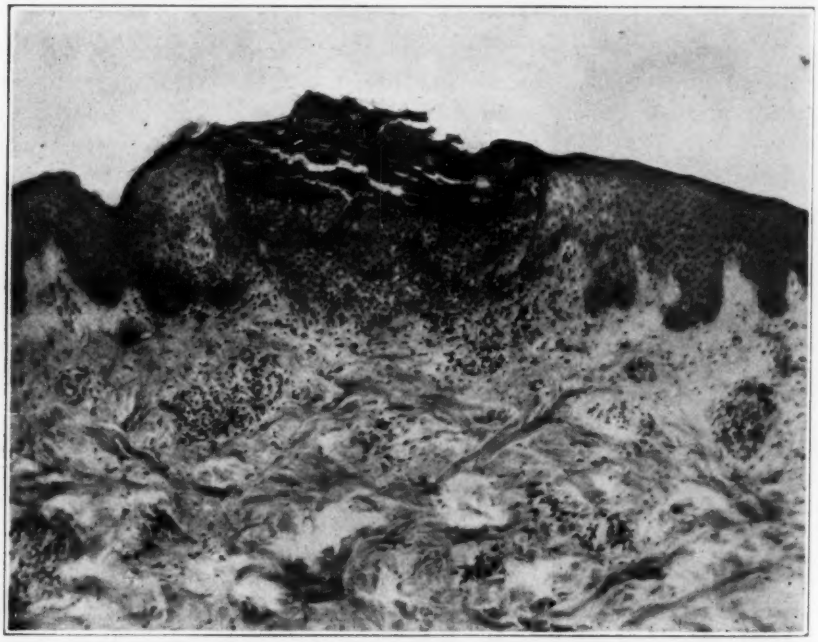

Fig. 3.—Nummular eczema. Note the cellular type of vesicle, regular acanthosis and focal cellular infiltration about the vessels. × 88.

cells, or both. There is little or no edema about the vesicle and this differentiates it from eczema. The remaining findings are those described under neurodermatitis.

However, similar vesicles are seen in other diseases. First, so-called pustular psoriasis is characterized by this type of vesicle, but within it are numerous polymorphonuclear leukocytes, many of them broken down. In other words, it is a true pustule. The more important distinguishing features are to be seen in the cutis. There is a mild inflammatory reaction in the subepidermic region, but this is chiefly in the area of the pustule, and the vessel walls are not involved.

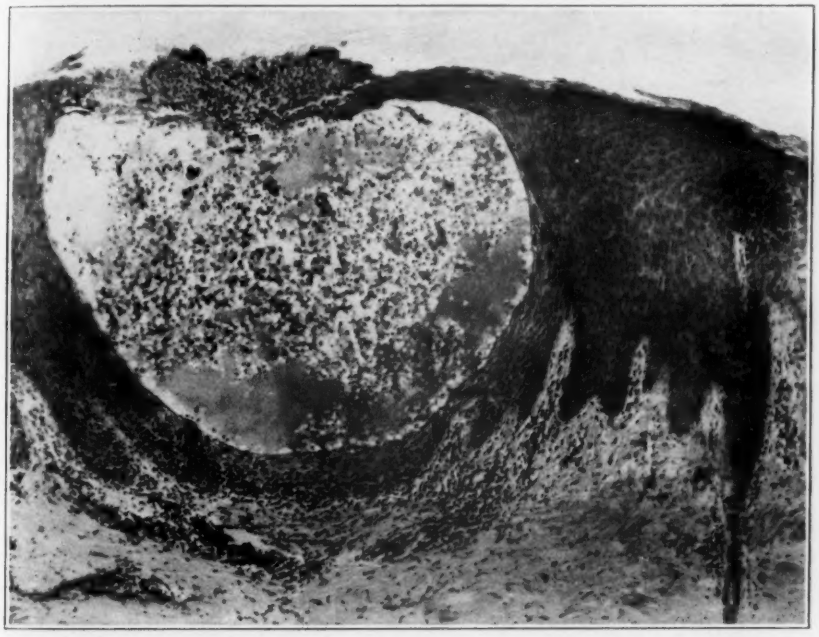

Fig. 4.—So-called pustular psoriasis. Note the true pustule containing polymorphonuclear leukocytes and cellular reaction about the vessels in the subepidermic region. × 88.

So-called pustular psoriasis is different from psoriasis with pustules. In the latter, one finds all the features of psoriasis, and the pustule is secondary, small and high in the epidermis. In so-called pustular psoriasis, the pustule is large, primary and may extend throughout most of the epidermis.

The second disease to be differentiated from nummular eczema is pompholyx. There are two types, one due to increase and retention of sweat and the other due directly, or indirectly, to a fungous infection. In the first, the vesicle contains only fluid, and at its base the opening of a sweat duct is visible. Thus it appears that this vesicle is due

primarily to some physiologic, rather than pathologic, process. It is true that the vesicle of the other variety of pompholyx also contains only fluid, but a sweat opening is not found. At times, a fungus can

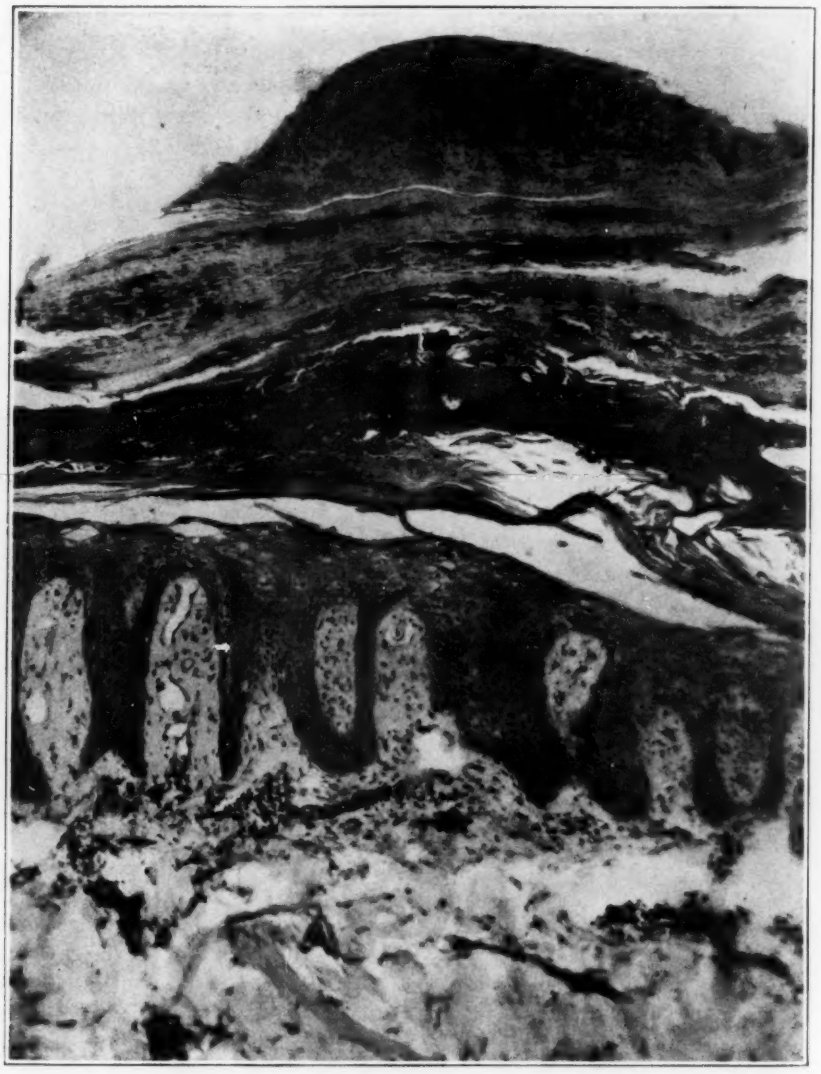

Fig. 5.—Psoriasis with pustules. Note typical picture of psoriasis with secondary pustulation. × 114.

be demonstrated. There is a mild diffuse inflammatory process in the upper cutis and subepidermic zone, and plasma cells may be present.

Finally, contact dermatitis should be considered with this group. The vesicles are usually small, numerous and at the surface of the

epidermis. They are filled with fluid, cells, or both. The cells are identical with those of the underlying inflammatory process, which is composed of small round and wandering connective tissue cells. The primary irritant type of contact dermatitis may have pustules, not only in the epidermis, but also in the cutis directly beneath the epidermis, and especially about the hair follicles and sweat ducts. The epidermis is not acanthotic.

EXUDATIVE LICHENOID AND DISCOID CHRONIC DERMATOSIS

In its different stages exudative lichenoid and discoid chronic dermatosis clinically may closely resemble pityriasis rosea, eczema, contact

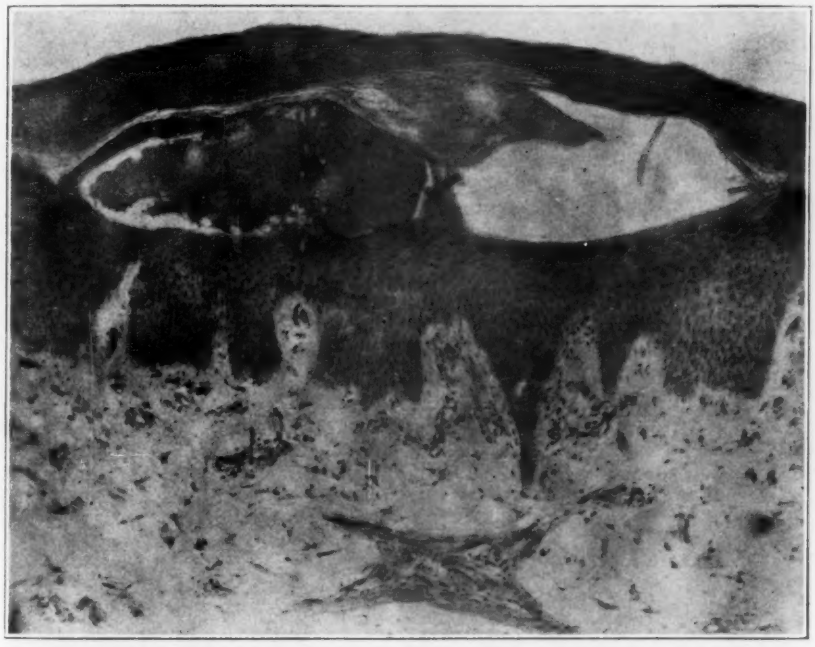

Fig. 6.—Pompholyx. Note vesicle containing fluid and a sweat duct at the base of the vesicle. The inflammatory reaction is mild and diffuse. × 88.

dermatitis, lichen planus, dermatitis herpetiformis, mycosis fungoides, exfoliative dermatitis, etc. The lesions and the entire general picture change from one phase to the other.

However, the many clinical variations may be explained by the intensity of the reaction, for the basic pathologic findings are fairly constant and conform to those of the neurodermatitic reaction. Although acanthosis may be slight, usually it is pronounced. In some stages edema may be slight, while in other phases it will be extensive, showing all gradations from basal cell disturbance to parakeratosis. Small super-

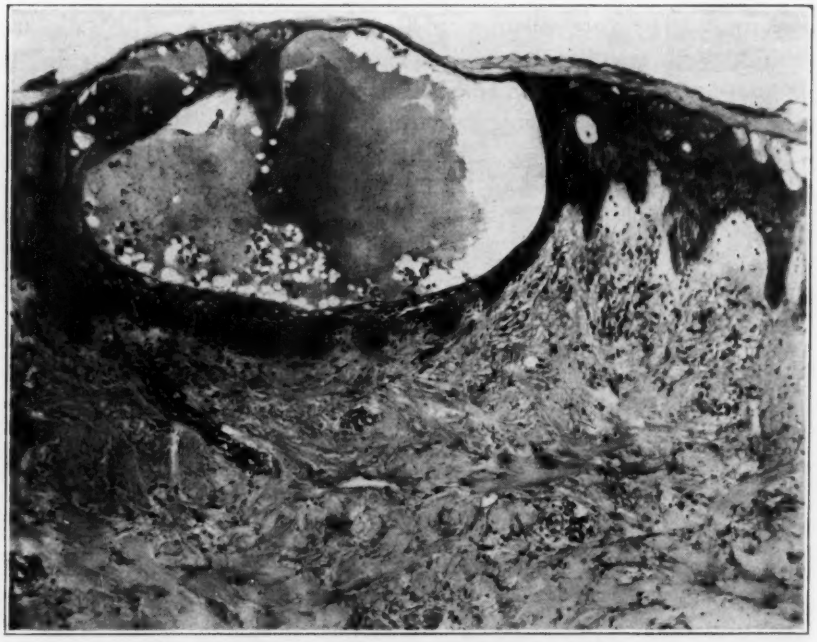

Fig. 7.—Contact dermatitis. Note the edematous type of vesicle containing a few cells that are identical with those of the underlying simple type of inflammatory reaction. × 88.

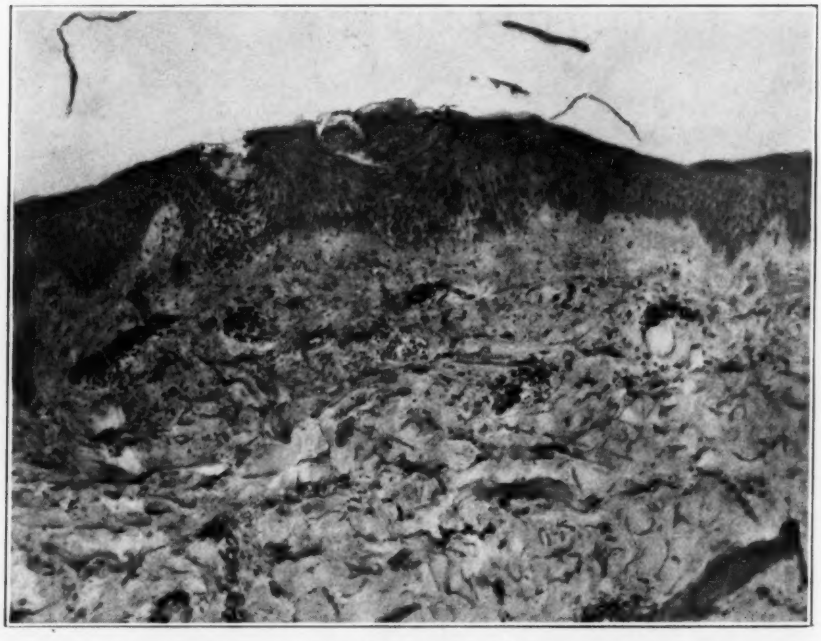

Fig. 8.—Contact dermatitis. Note the cellular type of vesicle. The inflammatory reaction is composed of small round and wandering connective tissue cells. × 88.

ficial vesicles simulating contact dermatitis may be present. The latter can be, and in fact often are, superimposed. When edema, not in the sense of eczematization, but of primary nature and part of the process, is found in the epidermis, it is important as a distinguishing feature of this group. However, the most striking feature of exudative lichenoid and discoid chronic dermatosis is the presence of plasma cells in the focal cellular infiltration which are found close to the vessel wall. Only an occasional epithelioid cell may be seeen.

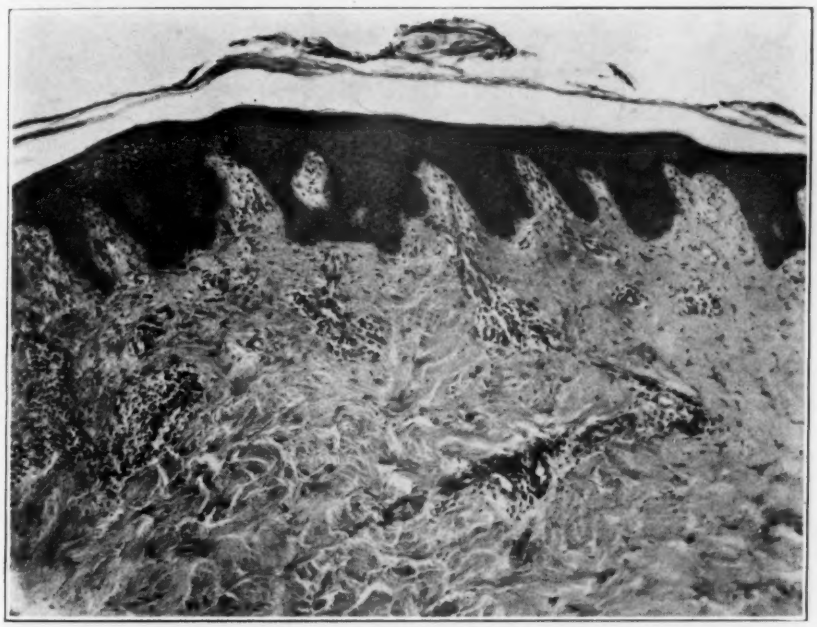

Fig. 9.—Exudative lichenoid and discoid chronic dermatosis. Note regular acanthosis and focal cellular infiltration about the vessels of the middle and upper layers of the cutis. × 88.

From this last disease, iodide and bromide lesions must sometimes be differentiated. This is not easy or always possible. In the early stages the epidermis is not involved, and the infiltration is composed chiefly of polymorphonuclear leukocytes and small round cells that at times resemble lymphocytes; the vessel walls are not thickened. Later, the cellular infiltration becomes extensive; there are many types of cells; liquefaction necrosis and, finally, granulation tissue appear.

Lymphatic leukemia should also be considered here. Differentiation is rather simple, as the epidermis is passive and the cellular infiltration is made up entirely of lymphocytes. These are of uniform size and round, but slightly larger than a small round cell and have a small

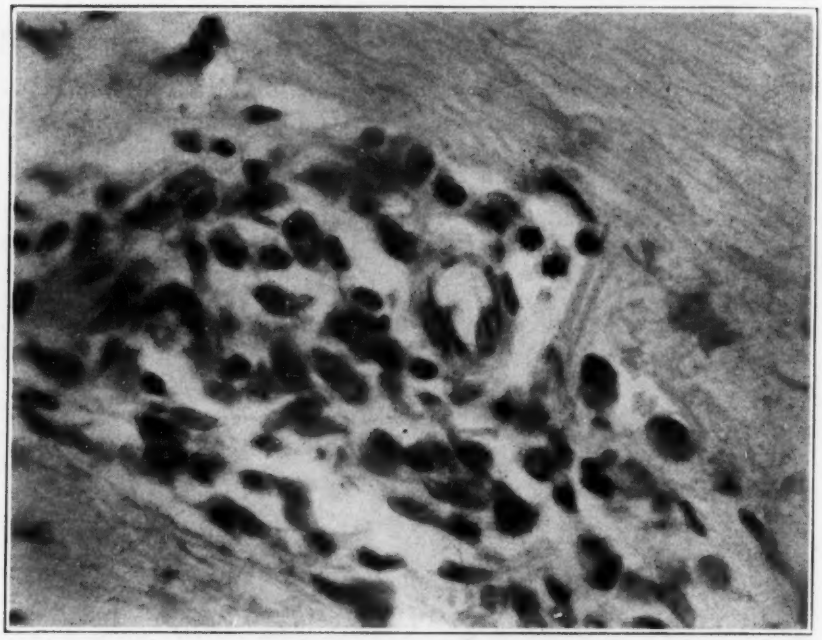

Fig. 10.—Exudative lichenoid and discoid chronic dermatosis. Note dilated vessels with thickened walls. Plasma, wandering connective tissue and round cells may be seen in the infiltration. × 944.

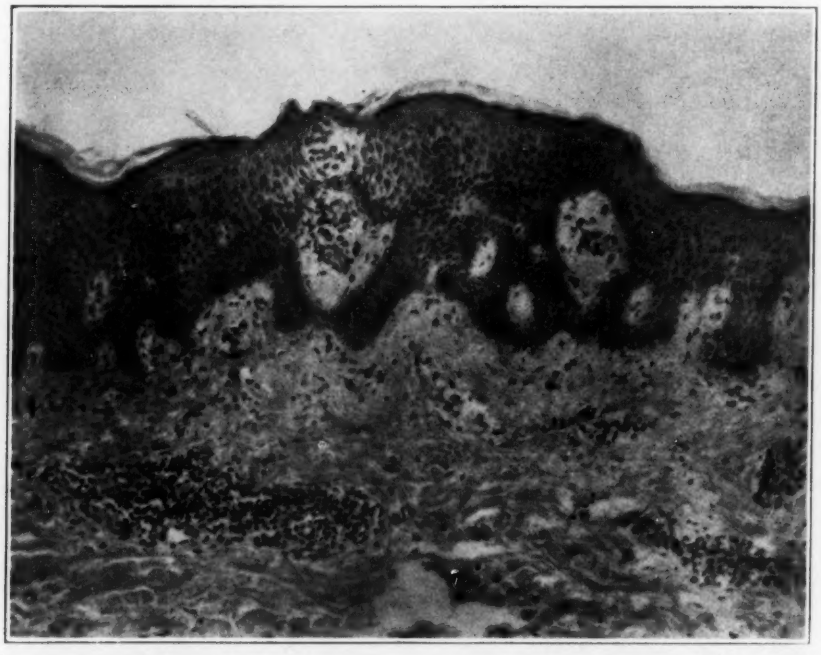

Fig. 11.—Mycosis fungoides. Note an acanthotic epidermis and focal cellular infiltration about the vessels. A Pautrier abscess may be seen in the upper part of the epidermis. × 116.

amount of cytoplasm about the nucleus. The nucleus is also round, and the chromatin is not densely packed.

The last and probably the most important disease to be considered in this group is mycosis fungoides. One of the reactions seen in the early stage suggests exudative lichenoid and discoid chronic dermatosis. The epidermis may show no characteristic change; if Pautrier's abscess is present, it is diagnostic. In the cutis the infiltration is focal about the vessels and, although other cells are present, the epithelioid cell predominates. In a well established lesion there are different types of cells, reticulum, grouping of the cells, breaking up of nuclear material, clumping of nuclei, mitotic figures and Pautrier's abscesses. When these other features of mycosis fungoides are present, they are of considerable aid in arriving at a diagnosis.

COMMENT

In both types of neurodermatitis there are the typical features described for the neurodermatitic reaction. Nummular eczema differs only in the presence of an intraepidermic vesicle. Exudative lichenoid and discoid chronic dermatosis is characterized by the type of cell in the focal inflammatory reaction. In the first two, the cellular infiltration is typical of an exudative inflammatory process; in the last group, it is of the productive variety. In all three, the walls of the arterioles and the small arteries are involved.

Clinically, there is a close relationship between these dermatoses. Patches of nummular eczema are seen in cases of neurodermatitis, and exudative lichenoid and discoid chronic dermatosis may at times suggest either disseminated neurodermatitis or nummular eczema. Incidentally, we believe that nummular eczema is of frequent occurrence, and that many more of the vesicular diseases of the extremities may belong in this group.

SUMMARY

A classification of the neurodermatitic reaction is presented. The dermatoses in this group may easily be confused, and only careful consideration of both the clinical and the microscopic features will establish a final diagnosis.

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A STUDY ON ULCUS PHAGEDENICUM CUTIS

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ULCERS of various origin, such as diphtheria, leishmaniasis cutis and tropical ulcers are rather common in the countries of the Near East, but in the years during which we have seen a number of them we have also frequently encountered a special sype which does not fit into any of the aforementioned categories.

Its distinction from the aforementioned ulcers is determined by its clinical aspect and by the bacterial flora it presents. In connection with the desert warfare in the Near East the problem has gained particular importance.

To characterize the cases which we have seen during the last ten years, it seems to us that the most appropriate term would be "phagedenic ulcer." This denotes a circumscribed inflammation of the skin which may lead to destruction of the entire cutis and subcutis down to the fascia, progressing in waves and on the whole running a chronic course, and occasionally new outbreaks being accompanied with reactions of a generalized nature. The ulcers do not tend to heal spontaneously.

We collected data on 58 cases, most of them in the last few years, a fact which may serve as an indication of the comparatively frequent incidence of the lesion in this and the neighboring countries. Thirty-three of the patients were admitted to our hospital, while 25 remained outpatients. Since for the latter it was impossible to make all the various tests and laboratory examinations, as some of the patients called irregularly and some of them only once, they were included only insofar as the data were considered relevant. With regard to the 33 inpatients, various systematic examinations could be made. In order to avoid tedious case histories, the data are summarized and characteristic illustrations attached.

In all our patients we found normal conditions with regard to the urine, feces, blood cell count, chemical analyses of the blood for urea, sodium chloride, glucose and, in the majority of cases, calcium. Wassermann and Kahn reactions were invariably negative except for

From the Dermatologic Department of the Rothschild-Hadassah University Hospital, Head, Dr. A. Dostrovsky.

those of 1 patient in whom the tests elicited slightly positive reactions. In some patients the gastric juice could be analyzed, and determinations made of vitamin C in the blood and urine. In others roentgenograms of the lungs, experiments with animals (tuberculosis) could be made, and blood sedimentation rate and basal metabolic rate could be determined. The results of these examinations showed wide variations, and no constancy could be established.

DISCUSSION OF THE MATERIAL

Clinical Appearance.—The first sign of the beginning ulcer is a sanguineous pustule surrounded by a bluish red discoloration of the skin. When the upper part is removed, one finds a greater degree of destruction in the depth than one would expect, judging by the outward appearance (fig. 1). The edges are already slightly undermined.

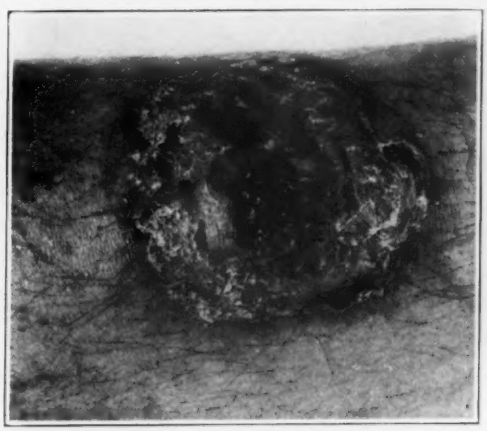

Fig. 1.—After removal of upper crust, a greater destruction in depth is shown than one would suspect.

In general, patients are rarely seen in that stage, as they usually seek medical advice only when the process has already reached the stage of extensive ulceration. In our patients the ulcers were on an average 5 to 6 cm. in diameter, some of them reaching a size of 15 to 20 cm. The floor was uneven, with additional slight depressions, and covered with a serous, occasionally mucopurulent or gelatinous, secretion which had an offensive smell, reminding one of the smell of raw meat. No considerable discharge from the surface was noted. The color of the floor was gray, sometimes slightly sanguineous.

The bluish red edges were extensively undermined, in typical cases the epidermis hanging down in curtain fashion, while below them the cutis as well as the subcutis had disappeared. This portion of the edge was found to be soft and brittle and of an even darker tinge.

Acute progression would occasionally occur by way of undermining corridors, in 1 case of 8 cm. in length, on an average, however, not exceeding 1 to 3 cm.

After some time, these corridors would open into new ulcerations in such a way that here subsidiary ulcers were formed. More or less wide bridges of normal skin remained either not involved at all or only later becoming necrosed.

The skin surrounding the ulcers was inflamed and swollen. In a great number of cases, starting from a line exactly coinciding with the outer margin of the undermined portion, the ulcers were surrounded by an area of superficial detachment of the epidermal layer.

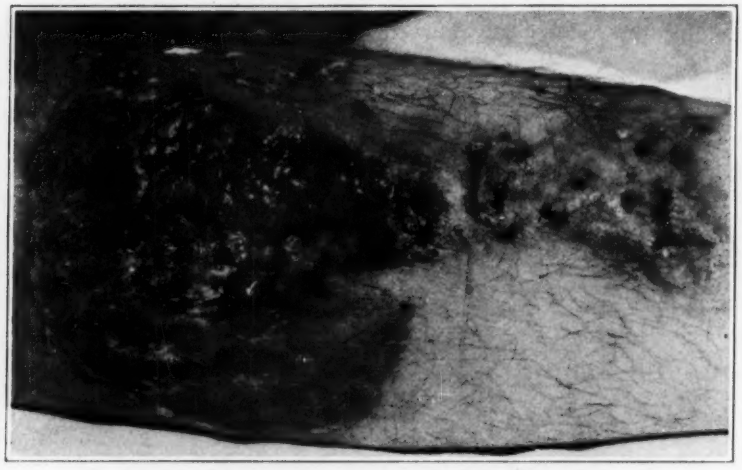

Fig. 2.—Lesion 15 cm. in diameter, ulcer being only 3 cm. in diameter.

In 1 of the patients such an area of detachment was 15 cm. in diameter while the ulcer itself occupied an area of only 3 cm. in diameter. Reference to this peculiar feature has not been found anywhere in the literature, although in our opinion it should be considered as one of the characteristics of that lesion. It is not yet clearly understood whether maceration or secretion or the invasion of germs may account for this superficial epidermal detachment. The outer edges of these areas showed, as a matter of fact, something in the nature of undermining, so that the original ulcer seemed to be reproduced in the shape of a superficial erosion.

As a rule, the ulcers occur singly and only rarely are two or more observed in the same person simultaneously. In the literature, however, cases of extraordinary severity have been described, multiple ulcers being present all over the body.

Location.—As a general rule, the lesions may be expected to occur anywhere on the skin—that is, anywhere that trauma may affect the skin and invasion of germs may take place. In our cases we noted predilection of certain locations. In the following table the location of the ulcers in 51 cases is recorded.

In no case was the localization that of varicose ulcers, found as an accompaniment of enlarged veins. The malleolar ulcers were always immediately on the osseous surface, occasionally spreading from there.

Since the majority of the patients were young, varicose veins rarely came into the picture at all; hence, the circulatory factor could be safely eliminated. It appears to be of far greater significance that out of fifty-one ulcers forty-one were found on the malleoli and tibias, i. e., on places where exposure to injury and pressure is particularly

TABLE 1.—*Location of Ulcers in Fifty-One Cases*

Location		No. of Cases
Malleolus		17
Medial	12	
Lateral	5	
Tibia		24
Lower third	17	
Upper portion	7	
Upper extremities		4
Mamma (fig. 9)		2
Inguinal region		1
Iliac region		1
Femoral region		1
Gluteal region		1
Total		51

great. Location, therefore, seems to be one of the essential factors in the causation of the lesion.

As to complications, there was erysipelas twice and in 2 cases necrosis of the tendons of the superficial extensor surfaces of the foot and of the achilles tendon. In a postoperative ulcer of the chest there was perforation into the pulmonary tissue.

Three of our patients died, 1 from pyopneumothorax and 2 after operative treatment of the ulcers in Europe and the United States of America, respectively.

Age.—The age distribution is given in table 2, showing a fair share of all age groups.

Out of 58 cases, therefore, in 48 the patients were under 40 years of age. The maximum frequency is found between 15 and 40. It should, however, be borne in mind that the age distribution of Palestinean Jews is an abnormal one in view of recent immigration, with prevalence of the younger groups. Immigrants were, by the way, found to be attacked by the disease in the same way as natives.

Sex.—Males outnumbered females by 30 to 28; a prevalence of the female sex could not, therefore, be established in our study, although, among the more severely involved patients who had to be admitted to the hospital 19 were women as compared to 14 men. The

Fig. 3.—Common site of lesion due to trauma.

Fig. 4.—Ulcer complicated by erysipelas, with necrosis of tendons.

majority of the patients were young, healthy, strong, normally built and in a satisfactory state of nutrition.

At the time of the patients' admission, the ulcers had been present for periods of from five weeks to one and a half years.

In 1 case colitis had preceded the development of the ulcer, and it recurred during the period of treatment. No amebas or tubercle

bacilli were found in the feces. In another case there was associated pellagra and in 2 others Bürger's disease. In the latter, no doubt, the underlying disturbance had to be held responsible for the production of the ulcer, but apparently streptococcic invasion had supervened so

TABLE 2.—*Age Distribution in Fifty-Eight Cases of Phagedenic Ulcer*

Age of Patient	No. of Cases
0 to 10 years	3
10 to 20 years	19
20 to 30 years	13
30 to 40 years	13
40 to 50 years	7
50 to 80 years	3
Total	58

Fig. 5.—Ulcus phagedenicum cutis.

that further development was perfectly parallel to that observed in our other patients.

In 25 cases traumatism could be traced as the exciting cause, while in the others the patients were unable to give any information as to causation. The primary injury was, as a rule, reported in the malleolar region or over the tibia and was caused by stones, iron, bicycle accidents, barbed wire, mosquito bites or, as in 1 case, a dog bite. Other causes were injection of milk, phlegmon or operation on deformed feet.

From the description of patients from whom intelligent information could be extracted the following characteristic picture emerged: The first injury was, as a rule, an ordinary contusion, occasionally accompanied with insignificant hematomas, without erosion of the skin. It was only after renewed trauma had involved the same place—some-

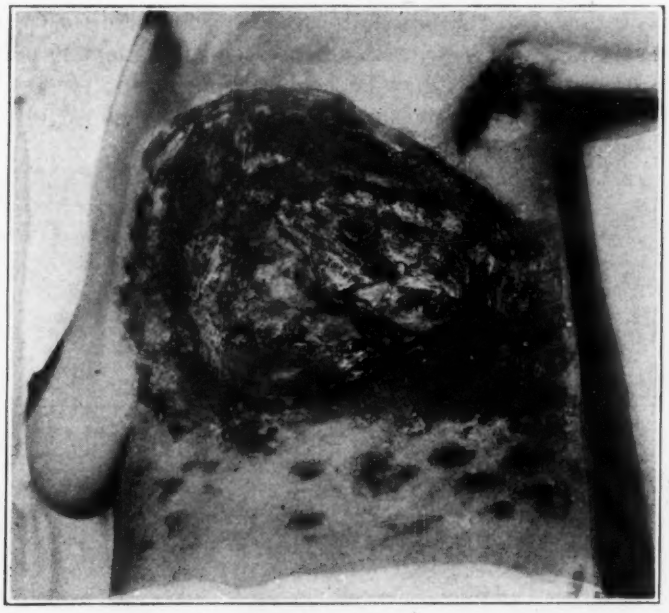

Fig. 6.—Ulcus phagedenicum cutis.

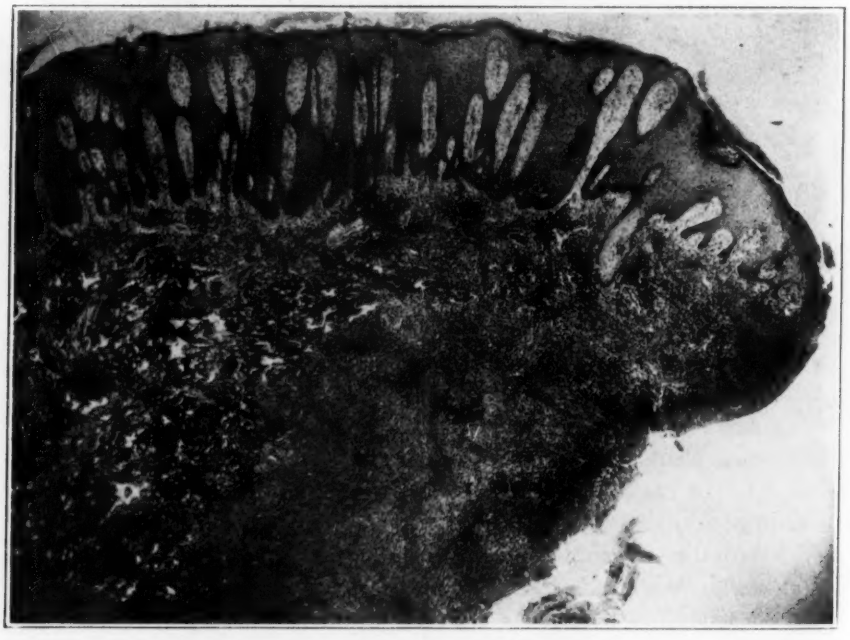

Fig. 7.—Acanthotic epithelium overlapping edges of ulcer. An acute inflammatory process in the cutis.

times weeks later with injury to the skin that the ulcers had developed and could not be brought to heal. Some of the patients, however, reported that the ulcers developed after the first injury.

Colitis was only once recorded as a forerunner in our cases, a situation not in accordance with the data published in the literature.

Bacteriology.—Extensive bacteriologic examinations were possible in 44 cases. Cultures were made on blood plates as well as on anaerobic culture mediums, on bouillon and agar. The procedure was to take material from the center of the ulcer and from underneath the undermined edges separately and to inoculate the portions separately into the culture mediums. It was seen that findings in the periphery substantially differed from those of the center. In fresh, not yet treated, cases hemolytic streptococci were the sole organisms, later disappearing from the center, where their place was occupied by Staphylococcus aureus, while in the recesses beneath the overhanging edges they continued to be present. In areas where corridors had developed, the skin over them was punctured and material aspirated from the depth with a syringe; hence, we were often able to obtain pure cultures of the bacterial flora of these corridors. In the 44 cases which were examined bacterial findings were the following:

	No. Cases
Hemolytic streptococci and Staphylococcus aureus	17
Hemolytic streptococci alone	3
Staph. aureus alone	7
Str. anaerobius and Staph. aureus	4
B. proteus and Staph. aureus	4
B. proteus alone	4
B. coli and Staph. aureus	1
Staph. albus and B. pyocyaneus	1
Staph. albus alone	1
Pneumococcus	1
Sterile	1
Total	44

In more than half the cases, therefore, hemolytic streptococci or Str. anaerobius was found in symbiosis with Staph. aureus or either of them separately. In this respect our results show a high degree of concordance with those collected by Touraine and co-workers [1] from the literature.

A definite parallelism could be established between bacterial findings and the course of the disease. As long as hemolytic streptococci were present, new spreading to the periphery was recorded again and again. In a number of cases the process would apparently come to a standstill peripherally, to be all of a sudden interrupted by new outbursts. As a response to therapeutic measures hemolytic streptococci were first to

1. Touraine, A., and Duperrat, R.: La gangrène post-opératoire progressive de la peau, Ann. de dermat. et syph. **10**:257-285 (April) 1939. Touraine, A.; Lortat-Jacob, E., and Neret: La gangrène microbienne insulaire bénigne de la peau, Bull. Soc. franç. de dermat. et syph. **45**:1022-1026 (June) 1938.

disappear, while Staph. aureus followed more slowly. Then occasionally B. proteus would make a transitory appearance for shorter or longer periods until the ulcer was eventually sterile. The observations tabulated are, for the greatest part, those of the initial stages, e.g., prior to treatment. If secondary contamination was suspected, we applied compresses soaked in isotonic solution of three chlorides, which were left on the ulcer for a few days, and now and then it was possible, after two to three days of this treatment, to obtain pure cultures of hemolytic streptococci or Staph. aureus.

Histologic Examination.—In 14 cases biopsy specimens were taken from the edges as well as from the floor of the ulcers. In the following paragraph is given the histologic report (Pathological Institute, Head: Professor Franco).

The histologic picture is that of chronic, subacute inflammation with ulceration but without evidence of specificity. The inflammatory process extends over the whole width of the specimen. Between the infiltrating cells there are fine epithelial bands isolated from each other by inflammatory tissue, giving the impression of a retrograde development.

In figure 1 one sees the epithelium overlapping the edges of the ulcer, with a tendency to grow into the depth. Microscopic conditions explain the aspect, as it presents itself to the naked eye, of an ulcer with undermined edges. The whole width of the cutis shows decided infiltration, indicating a subacute inflammatory process (plasma cells, histiocytes, leukocytes and a few granulocytes). The granulocytes are in particularly great number present at the edges of the ulcer together with red blood corpuscles, their number and distribution varying from one place to the other.

Figure 8 shows an area of subcutaneous adipose tissue, with particularly decided inflammation. Note the extensive cell infiltration.

Differential diagnosis.—During the desert war in the Near East a number of ulcerations reported were generally included in the group of "desert sores." In reality, they represent ulcers of widely varying causation but in the main belonging to the three well known groups: tropical ulcers, diphtheritic ulcers and those called by us[2] "phagedenic ulcers." The distinction of the last from tropical ulcers seems to be the most important issue from the differential diagnostic standpoint. Ulcus tropicum fusospirillosum also develops in the malleolar or tibial region, likewise appearing singly. Its floor is, however, covered with a dirty gray gelatinous membrane; it is of oval shape and sharply outlined with no undermining of the edges. It causes, moreover, extraordinarily violent pain so that often narcotics have to

2. Dostrovsky, A., and Sagher, F.: Phagedenic Ulcer (Pyoderma Gangraenosum): Treatment with Sulfapyridine Powder and Moist Chamber Therapy. Arch. Dermat. & Syph. **48**:164-172 (Aug.) 1943.

be taken. Kerby [3] identified spirochetes as well as fusiform bacilli, micrococci and other bacteria in them, and so did Brown [4] in half the number of his cases. In this country the disease has been studied by Garry,[5] Berlin [6] and Blum,[7] whose publications on the subject contain much valuable information.

Although bacteriologic specimens were again and again studied by us, we were in no case able to detect spirochetes or fusiform bacilli. In the great number of references to the lesion found in the literature,

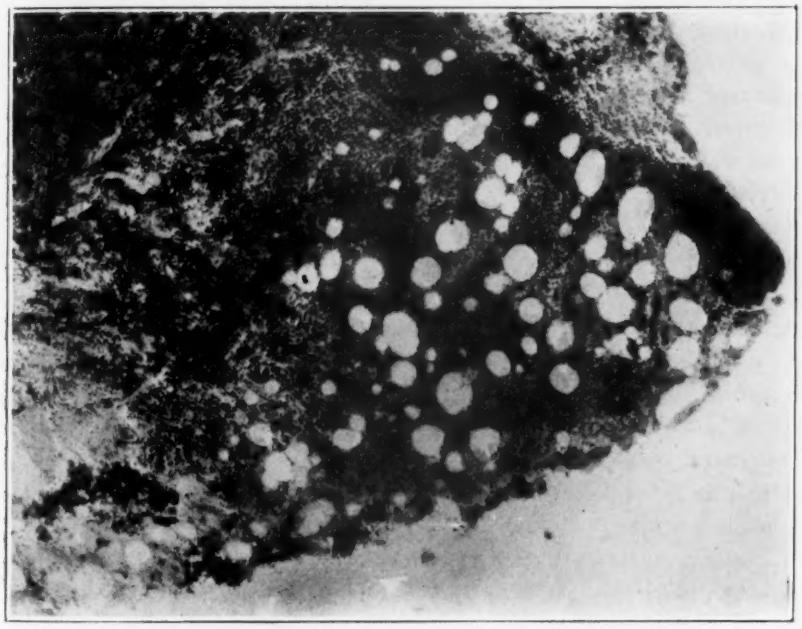

Fig. 8.—Decided inflammation in adipose tissue.

particularly from tropical regions, now and then the two types seem to have been confused and included in one and the same group under the heading "tropical ulcer." That the two types are, however,

3. Kerby, T. R. F.: Ulcus Tropicum, Lancet **1**:235-237 (Jan. 30) 1932.

4. Brown, A. A. F.: Ulcer Syndrome in Tropical Africa, J. Trop. Med. **38**:157 (July 1) 1935; 170 (July 15) 1935; 187 (Aug. 1) 1935; 201 (Aug. 15) 1935; 215 (Sept. 2) 1935.

5. Garry, G.: Ulcus Epidemicum, Arch. f. Schiffs- u. Tropen-Hyg. **34**:351-354 (July) 1930.

6. Berlin, C.: Ulcus Tropicum and Its Treatment: Report of Epidemic 1934, Harefuah **11**:ii-iii (Nov.) 1936.

7. Blum, I.: (*a*) A Seldom Form of Chronic Ulcer of Skin Due to Streptococcus Micro-Aerophilus, Harefuah **23**:153-154 (Nov. 15) 1942; (*b*) The Differential Diagnosis of Some Infectious Ulcers of the Skin, ibid. **25**:90-91 (Sept. 1) 1943.

definitely different as to their pathogenesis is shown by experiments conducted by Smith,[8] who was able to produce tropical ulcers by inoculation of cultures of fusiform bacilli and spirochetes.

Diphtheritic ulcers, which in the subtropical zones are not rare, may be recognized by the slight or altogether absent undermining of the edges, which are, as a rule, thickened; further by their constant shape and the grayish membrane with which they are covered, often firmly attached to the floor, as well as by the slight degree of discharge from the surface.

A similar aspect is presented by the so-called "pyodermia chancriformis faciei" (Hoffmann[9]), although this lesion is more superficial, indurated and accompanied with distinct swelling of the lymph nodes. Moreover, localization in the face has never been encountered in our cases, while in the type referred to by Hoffmann[9] it is characteristically restricted to that region.

What has been described as "pyoderma gangrenosum" (Brunsting, Goeckerman and O'Leary[10]) presents conditions, clinically as well as bacteriologically, similar to those found in our cases. Whether the lesions described by Meleney[11] can be distinguished from those of our group on the grounds of the slight deviations in their clinical picture is doubtful. Probably the two lesions represent variations of one and the same process, which have been named differently. Postoperative progressive gangrene has, therefore, also been included by us in this group. In the same way as is the case with spontaneous ulcers it is caused by trauma, here provided by operation.

Meleney[11] and Cullen[12] reported lesions of this type on the abdomen, particularly occurring after drainage of abscesses or empyema,

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8. Smith, E. C.: Inoculation Experiments with Bacillus Fusiformis Isolated from Tropical Ulcer with Observations on Bacillus, J. Hyg. **33**:95-102 (Jan.) 1933.

9. Hoffmann, E.: Isolierte schankeraehnliche Pyodermie der Gesichtshaut (Pyodermia chancriformis faciei), Arch. f. Dermat. u. Syph. **170**:403-409, 1934.

10. Brunsting, L. A.; Goeckerman, W. H., and O'Leary, P. A.: Pyoderma (Ecthyma) Gangrenosum: Clinical and Experimental Observations in Five Cases Occurring in Adults, Arch. Dermat. & Syph. **22**:655-680 (Oct.) 1930.

11. (*a*) Meleney, F. L.: Hemolytic Streptococcus Gangrene, Arch. Surg. **9**: 317-364 (Sept.) 1924; (*b*) Differential Diagnosis Between Certain Types of Infectious Gangrene of Skin, with Particular Reference to Haemolytic Streptococcus Gangrene and Bacterial Synergistic Gangrene, Surg., Gynec. & Obst. **56**:847-867 (May) 1933. (*c*) Meleney, F. L., and Johnson, B. A.: Further Laboratory and Clinical Experiences in Treatment of Chronic Undermining, Burrowing Ulcers with Zinc Peroxide, Surgery **1**:169-221 (Feb.) 1937.

12. Cullen, T. S.: Progressively Enlarging Ulcer of Abdominal Wall Involving Skin and Fat, Following Drainage of Abdominal Abscess Apparently of Appendiceal Origin, Surg., Gynec. & Obst. **38**:579-582 (May) 1924.

as well as after drainage of the armpit. Schmidt's [13] case presented colitis and carcinoma, and it was in the operative wound that the gangrenous ulcer appeared—a similar development is found in 1 of our cases.

In our case, after operation for mammary carcinoma with subsequent drainage, an ulcer developed, which in the course of two and a half months laid bare the whole of the chest wall on the right side and, apart from a disastrously progressive tendency and extensive undermining of the edges, spread also to the depth, leading to pyopneumothorax with erosion of small blood vessels to which the patient eventually succumbed (fig. 9).

Fig. 9.—Ulcer developing two and a half months after operation for carcinoma.

Therapy.—After initial attempts to influence the ulcers by zinc peroxide treatment, the onset of the sulfanilamide era induced us to start oral and intramuscular as well as local sulfanilamide therapy too, and we saw rapid disappearance of the bacterial flora from the ulcers treated by this method. When sulfanilamide, sulfapyridine or sulfathiazole powders are employed, it is imperative that an intimate contact be established between the powder and the parts to be treated. The powder should be introduced in a way that actually insures its reaching all the nooks and corners beneath the undermined edges of the ulcer, by a sound or spatula, deep underneath the overhanging edges, and

13. Schmidt, H. W.: Hyperimmune Streptococcic Serum in Treatment of Pyodermia Gangrenosa Associated with Chronic Ulcerative Colitis and Carcinoma of Colon, Proc. Staff Meet., Mayo Clin. **11**:244-247 (April 15) 1936.

applications should be repeated every twenty-four hours, until the ulcer has been rendered sterile, which, as a rule, requires three weeks. To stimulate granulation, we employed the moist chamber method. Although this was no "quick method," it was possible to get the disease under control and to forestall further outbreaks so that in the end retrogression could be enforced. It became, moreover, clear that removal of the undermined edges by means of surgical manipulations was unnecessary, since the detached parts often grew together again.

COMMENT

Reference to the disease is found in the literature under many different designations, from Brocq [14] up to very recent times, but neither the clinic, the pathogenic nor the bacteriologic study yields a uniform picture. It is not only under different designations but under one and the same, too, that wide variations have been described. It is our endeavor, by including characteristic photographs showing the lesion at various sites and giving a good illustration of its special properties, to outline a typical picture of the disease, thus facilitating its distinction from other diseases.

There is no consensus as to what persons are generally attacked by the disease. Touraine and co-workers [1] stressed its preponderant occurrence in women over 50 years of age, while Cohen [15] drew attention to its prevalence in young girls. Meleney,[11] on the other hand, pointed out that the lesion may be encountered at any age, in an equal measure in both sexes and anywhere on the body surface. Our material does not give any indication as to the prevalence in one sex or a special age group either but gives evidence of predilection for the malleolar and tibial regions, although any other part of the body may equally be attacked.

As to the existing cause, opinions are also at variance. Sachs [16] saw an ulcer of this kind develop in a girl who showed no constitutional stigmas and, after the lapse of four years, heal in an equally inexplicable manner. Meleney,[11] Sutton [17] and Touraine and co-workers [1] report occurrence subsequent to traumatism, with no previous circulatory disturbance being reported in the areas involved. The trauma may

14. Brocq, L.: Nouvelle contribution à l'étude du phagédénisme géométrique, Ann. de dermat. et syph. **6**:1-39 1916-1917; cited by Greenbaum.[26]

15. Cohen, M. H.: Pyoderma Gangraenosum: A Deficiency Disease Complex, Arch. Dermat. & Syph. **33**:813-824 (May) 1936.

16. Sachs, W.: Sphaceloderma: Report of Case of Unusual Phagedenic Ulceration of Skin, Subcutaneous Tissue and Muscle of Chest Wall, Arch. Dermat. & Syph. **33**:977-987 (June) 1936.

17. Sutton, R., and Sutton, R., Jr.: Diseases of the Skin, ed. 9, St. Louis, C. V. Mosby Company, 1935.

be a mechanical one; it may also be provided by burns or operations. The majority of authors concerned with the subject describe their occurrence simultaneously with or as a consequence of chronic colitis. Jankelson and McClure [18] gave details of 7 cases of chronic idiopathic ulcerative colitis in which cutaneous ulcers developed when the infection was at its peak, in 4 cases disappearing during remissions of the underlying disease.

In the cases of Brunsting, Goeckerman and O'Leary [10] associated colitis was reported four times and empyema once. Weiner's [19] patient was also suffering from colitis, and Barger [20] found, among 150 cases of colitis, 12 which presented phagedenic ulcers. McCarthy [21] pointed out that the state of reduced resistance, created by colitis of prolonged duration, favors the development of large ulcers of the skin. It is possible that in patients suffering from colitis inadequate absorption may lead to vitamin deficiency, which does not, however, imply that the ulcers should be considered a direct consequence of this deficiency. Cohen [15] maintained that colitis, ulcers and hypochromic anemia form a pathologic triad. In his case there was atrophy of the tongue; the disease could not, however, be influenced by vitamin administrations, as he assumed, owing to the disturbed intestinal absorption. The majority of our patients were otherwise healthy, with no constitutional stigmas presenting evidence of internal disease.

There is a greater agreement of opinion in regard to bacterial findings. Although the number of germs held responsible for the production of the lesion is large, attention is in an increasing measure being focused on the fact that certain bacterial groups, either separately or in combination, are of vital importance. Brunsting and co-workers,[10] Brewer and Meleney [22] and Fox [23] attached particular significance to the symbiosis of hemolytic streptococci and Staph. aureus. Touraine and co-workers [1] gave a tabulation of 81 cases from the literature, 38 of which showed streptococci and staphylococci in symbiosis, while in 16 streptococcus occurred in combination with other nonstaphylococcic infections, and, eventually, in 8 cases, staphylococci were found in pure culture or in combination with other nonstreptococcic germs.

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18. Jankelson, I. R., and McClure, C. W.: Skin Lesions During Course of Ulcerative Colitis, Acta dermat.-venereol. **21**:255-267 (March) 1940.

19. Weiner, A. L.: Pyoderma Gangraenosum Treated with Sulfanilamide: Report of Case, Arch. Dermat. & Syph. **41**:711-717 (April) 1940.

20. Barger, J. A., in discussion on Schmidt.[13]

21. McCarthy, L., and Fields, R.: Pyoderma Gangrenosum, New York State J. Med. **31**:801-804 (July 1) 1931.

22. Brewer, G. E., and Meleney, F. L.: Progressive Gangrenous Infection of Skin and Subcutaneous Tissues, Following Operation for Acute Perforative Appendicitis: Study in Symbiosis, Ann. Surg. **84**:438-450 (Sept.) 1926.

23. Fox, H., in discussion on Cipollaro.[28]

Lane and Stroud [24] found hemolytic Staph. albus and streptococci, while Gibson [25] found Staph. albus only. Greenbaum,[26] who devoted a great amount of attention to this question, came to the conclusion that possibly streptococci and staphylococci act in conjunction but only if certain particular conditions are fulfilled, allowing the germs to display their activity and to produce the disease. Greenbaum [26] reported on 6 cases with similar bacterial findings. By inoculation it was possible to produce similar ulcers in the same patient at distant sites with streptococci and staphylococci in association but not, however, with one of the strains alone. In 1 case hemolytic Str. aureus and B. proteus, inoculated separately, provoked no reaction; in combination, however, they produced an ulcer, from the surface of which the two germs could even be recultured. In 1 of our cases, for experimental reasons, material taken from underneath the undermined edges of the ulcer where hemolytic streptococci had been identified, was applied to a scratch on the skin at a considerable distance from the original ulcer. The same procedure was adopted with material from the center (Staph. aureus), and eventually a mixture of the two materials was applied to a third scratch. All the experiments, although each one was repeated twice, yielded negative results, i. e., there was no local reaction at all to the inoculations.

Brewer and Meleney [22] stated the belief that the significance of the bacterial flora lies in the fact that hemolytic streptococci prepares the ground for the activity of Staph. aureus, which then continues the work of destruction. Bloom [27] does not support the etiologic röle of the bacterial flora, but stresses the importance of the presence of other diseases such as syphilis, tuberculosis, colitis and, in the case demonstrated by Cipollaro,[28] meningitis and mastoiditis.

A certain amount of significance might be attached to experiments on animals set up to clarify the question. Brunsting and co-workers,[10] using a combination of the two germs, were able to produce ulcers in their experimental animals similar to those found in human beings. Brewer and Meleney [22] found it possible to produce in guinea pigs and in rabbits and, in one instance, in a dog ulcers by combined inoculations

24. Lane, C. W., and Stroud, C. M.: Pyodermia Gangrenosum: Report of Case, Arch. Dermat. & Syph. **27**:460-471 (March) 1933.

25. Gibson, R.: Pyoderma Gangrenosa, Brit. J. Dermat. **49**:560-563 (Dec.) 1937.

26. Greenbaum, S. S.: Phagedaena Geometrica (Brocq): Inoculation Studies with Viable Bacteria Cultured from Lesions of Phagedaena Geometrica (Brocq) (Chronic Burrowing Ulcer and Pyoderma Gangraenosum), Arch. Dermat. & Syph. **43**:775-801 (May) 1941.

27. Bloom, D., in discussion on Cipollaro.[28]

28. Cipollaro, A. C.: Pyoderma Gangraenosum, Arch. Dermat. & Syph. **43**: 860-862 (May) 1941.

of nonhemolytic microaerophilic streptococci and hemolytic Str. aureus. Any of these strains applied separately rarely produced gangrene in the case of Staph. aureus, while with streptococcus this was altogether impossible.

Lane [29] successfully employed Str. hemolyticus vaccine (intracutaneously) in a concentration of 1:1,000 to provoke specific cutaneous reactions.

Whether special etiologic significance should be attached to the bacterial flora is, therefore, not altogether clear in view of the aforementioned data. The results of our own bacteriologic examinations were varied enough, although there was a definite preponderance of streptococci and staphylococci either alone or in symbiosis with each other. Our tabulation gives no indication of the frequency with which B. proteus has been encountered. Though in the initial stage it is not frequently met with, in the majority of cases it makes its appearance in the course of time. It may well be that it is initially suppressed by staphylococci and streptococci. Another striking feature is, moreover, the stubborn resistance of B. proteus against any attempt of therapy once it has established itself on the ulcer. The therapeutic measures instituted to influence the streptococcic flora had only one clear result in that it was only after their departure that the ulcer could be induced to heal.

The question as to why healing of these ulcers constitutes such a difficult problem is, therefore, still unanswered. A possible explanation may be that the activity of streptococci consists in a certain influence on the blood vessels, thus interfering with the supply of blood to the areas involved. On the other hand, the first injury may be the cause of the primary cellular lesion so that later supervening bacterial invasion may display its full weight. The matter is certainly rather intricate, which is characteristically illustrated by the following case history.

The patient was a boy of 14 who had always been healthy. Two years earlier he had, however, had osteomyelitis of the hip joint region which was cured but with reduced mobility of the joint. Three months before we saw him he fell and hurt himself in the neighborhood of the left trochanter where swelling subsequently developed. This swelling was punctured by a surgeon, and some blood withdrawn. Later, however, puncture revealed pus. A few days later an ulcer developed at the place of the injury, spreading geometrically and eventually reaching a size of 5 to 6 cm. The edges appeared as though they were punched and were extensively undermined down to the fascia. There was no swelling of lymph nodes nor pain.

29. Lane, C. G.: Spontaneous Necrotic Dermatitis (Hemolytic Streptococcus), Arch. Dermat. & Syph. **41**:414-415 (Feb.) 1940.

The patient had been treated with sulfanilamide at the surgical department. When he was admitted to the dermatologic department, bacteriologic examination revealed Staph. aureus.

As is seen from the history there had originally been an injury, but the surgeon in charge of the case reported that the skin had been unchanged up to the time of the first puncture. In this patient we might consider the possibility that we are dealing with a tissue reaction on the lines of the Shwartzman [30] phenomenon, arising on the grounds of the previous osteomyelitis.

SUMMARY

1. Details are given of 58 cases of a chronic ulcerative disease, consisting in the main of progressive, destructive lesions of the skin, occasionally down to the fascia, with deeply undermined edges. The ulcers appear in various locations, preponderantly the lower extremities, and usually in otherwise healthy persons. The outstanding feature of these lesions is phagedenization; hence, we propose the name "phagedenic ulcer."

2. Differential diagnostic distinction of the lesion from other ulcers occurring in subtropical regions is discussed. They should be distinguished from diphtheritic ulcers with their grayish membranes, absence of progressive spread and characteristic microscopic changes. On the other hand, a distinction should be made from tropical ulcers with their characteristically circular outline, foul-smelling slough, rapid development and typical micro-organisms.

3. Attention is drawn to the possibility of a similarity of this disease to pyoderma gangrenosum or Meleney's ulcer, in spite of the absence of gastrointestinal symptoms, the variety in the clinical aspect and the occasional absence of the typical bacterial flora described for the two last-mentioned diseases.

4. It is emphasized that the factors known to be relevant to the causation of the disease have only pathogenetic significance, and we maintain that there may still be another, as yet unclarified, etiologic factor.

Professor Franco, Head of the Institute of Pathological Anatomy, and Dr. Gurevitch, Head of the Bacteriological Department, both of the Rothschild-Hadassah University Hospital, assisted in the bacteriologic and histologic examinations.

30. Shwartzman, G.: The Phenomenon of Local Skin Reactivity to Streptococcus Hemolyticus-Scarlatinae, J. Infect. Dis. **48**:183-188 (Feb.) 1931.

VITAMIN B COMPLEX IN THE TREATMENT OF LICHENOID DERMATITIS

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A LARGE number of cases of dermatologic diseases developed among the American troops stationed on the Southwest Pacific island of New Guinea and the small islands adjacent for a radius of several hundred miles in the years 1943, 1944 and 1945. In this group of skin diseases a lichenoid form of dermatitis stood out as a major medical problem. It usually appeared in persons who had been in New Guinea for at least three months and in most cases on an average of nine to twelve months or longer. The soldiers affected had been taking quinacrine hydrochloride (atabrine) regularly for the suppression of malaria and were living solely on K or C rations for months at a time under field conditions in the tropical jungle, and fresh meat, vegetables and fruits were practically never included in their diets. Almost all the patients had lost from 10 to 40 pounds (4.5 to 18 Kg.) of weight after reaching the tropics. The same disease was seen in other war theaters where soldiers were taking quinacrine hydrochloride.

The eruption usually began on the hands or feet or simultaneously on both hands and feet as a simple patch of erythema alone or as erythematous patches with vesicles and pruritus. In most cases the lesions would at first be mild and remain localized for weeks or months, and then some extension would take place to other adjacent areas, or when the disease was severe, to the entire body. The lesions on the hands and feet were chiefly localized to the dorsal surfaces, and the distribution was suggestive of pellagra. The eruption often went through an exudative moist phase in the first few months, followed by a drying of all the moist areas and the production of three distinct types of morphologic entities thereafter. The commonest type was a severe dry scaling patchy erythematous dermatitis scattered over the dorsal surfaces of the hands, feet, legs, forearms and other areas of the body. This resembled a subacute eczema in its appearance and has been com-

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monly called eczematoid dermatitis. A second common type was a violaceous nodular and papular lichen planus form of eruption with pronounced pigmentary changes of the skin and lesions of the mucous membrane typical of lichen planus. This type clinically resembled severe hypertrophic lichen planus and was often generalized in distribution. The third, or mixed, type was a combination of the lesions of the eczematoid and lichen planus types in the same patient. All three types itched severely, often had a moist oozing phase and became secondarily infected and frequently went on to a generalized severe exfoliative dermatitis. In most cases the eruptions were resistant to any type of treatment employed in the New Guinea area, and a large number of the patients were returned to the United States. Many patients had clearing or improvement of their eruptions while en route to the United States, or recovery following treatment in various army general hospitals in the United States after their return.

Because of the distribution and pellagra-like appearance of some of the lesions; the lack of fresh fruits, vegetables, eggs, milk and meat in the diet for long periods; the tendency of the soldiers to eat native foods instead of rations balanced in vitamin content, and the common tendency to eat inadequate amounts of rations, we suspected that avitaminosis might play a part in the cause of the dermatitis or be a contributing factor in prolonging the eruption. Consequently, it was decided to survey all patients admitted to the dermatologic ward at DeWitt General Hospital by means of a form which summarized each patient's entire history and course of hospitalization. This form included the date of onset of the cutaneous lesions, the dates of hospitalization in New Guinea, a description of the lesions at onset as to type, location, development and subsequent distribution and the type and duration of the field diet overseas, with a notation of the presence or absence of fresh foods, any history of malaria, dysentery, secondary infection of the dermatitis, fever, edema and loss of weight and the general physical condition overseas. Abnormal laboratory observations, the type of treatment overseas, the dose of quinacrine hydrochloride and the duration of quinacrine therapy were also noted. On admission to DeWitt General Hospital each patient was photographed, and biopsies of the cutaneous lesions were taken. The course in the hospital, including the details of the treatment employed, was recorded daily. The 48 patients studied were divided into two groups, chosen alternately, both of which received routine standard dermatologic care, the details of the therapy depending on the type of case as previously noted and whether the stage of the disease present was acute, subacute or chronic. This local dermatologic care consisted of compresses, soaks, lotions, pastes and simple ointments, the exact treatment varying with the individual indications in each case. Roentgen ray therapy was employed in two thirds of the cases.

in which the chronic lichenified lesions responded slowly to local treatment. One of the two groups received, in addition to the local therapy, the following regimen of vitamin B complex therapy: (*a*) tablets, thiamine hydrochloride, 5 mg. twice daily; (*b*) yeast tablets, 3 Gm. daily; (*c*) riboflavin, 5 mg., with nicotinamide, 200 mg. (Lilly [1]) daily, intramuscularly; (*d*) extract of liver (Lederle concentrate, 10 units per cubic centimeter) 2 cc. intramuscularly, three times weekly, and (*e*) raw liver, 100 Gm. daily, specially prepared by the dietitian to promote palatability. At the time this treatment was instituted, all the patients had had their cutaneous lesions for from four to eighteen

TABLE 1.—*Summary of Data on Patients with Lichenoid Dermatitis Receiving Routine Dermatologic Care (Group I)*

Patient Number	Type of Eruption	Duration of Disease, Months	Severity	Time in Hospital, Weeks
1	Lichen planus	15	Severe	12
2	Eczematoid	11	Severe	16
3	Eczematoid	7	Severe	16
4	Lichen planus	9	Moderate	10
5	Lichen planus	12	Moderate	11
6	Lichen planus	18	Moderate	6
7	Eczematoid	5	Moderate	10
8	Eczematoid	7	Moderate	8
9	Lichen planus	3	Moderate	5
10	Eczematoid	8	Moderate	8
11	Eczematoid	6	Moderate	5
12	Lichen planus	5	Moderate	9
13	Eczematoid	3	Moderate	7
14	Eczematoid	6	Moderate	4
15	Eczematoid	7	Moderate	13
16	Eczematoid	9	Moderate	5
17	Eczematoid	6	Mild	8
18	Eczematoid	8	Mild	4
19	Eczematoid	11	Mild	6
20	Eczematoid	15	Mild	7
21	Eczematoid	5	Mild	9
22	Eczematoid	8	Mild	4
23	Eczematoid	3	Mild	5
24	Eczematoid	4	Mild	8
25	Eczematoid	9	Mild	4
26	Eczematoid	6	Mild	5

months. None of them were taking quinacrine hydrochloride. For purposes of comparison, the eruptions of all of the 48 patients were graded into three groups, mild, moderate or severe, depending on extent and severity. The patients with mild eruptions were those with lesions on the hands or feet alone or on both hands and feet. Those graded as having moderate eruptions had lesions involving one third to one half of the body area, while those with severe eruptions had extensive generalized and severe involvement.

Of the 48 patients who were included in this study 22 (group II) of them received the vitamin B complex regimen in addition to their local dermatologic treatment, and 26 (group I) received only the local

1. Riboflavin with nicotinamide ampules were furnished through the courtesy of Eli Lilly and Company, Indianapolis.

dermatologic treatment. Group II consisted of 4 patients with severe eruptions, 11 with moderate eruptions and 7 with mild eruptions, with an incidence of lichen planus lesions as follows: 1 with severe eruptions, 3 with moderate eruptions and 1 with mild eruptions. All the others had lesions of the eczematoid type except 1 with a severe eruption which was a generalized exfoliative dermatitis. In the control series of 26 patients (group I) there were 3 with severe eruptions, 13 with moderate eruptions and 10 with mild eruptions. One of the severe eruptions was of the lichen planus type, and five of the moderate eruptions were also lichen planus in type. There were no patients with mild lichen planus lesions in this group. No patient with a mixed type of

TABLE 2.—*Summary of Data on Patients with Lichenoid Dermatitis Receiving Routine Dermatologic Care and Supplemental Vitamin B Complex (Group II)*

Patient Number	Type of Eruption	Duration of Disease, Months	Severity	Time in Hospital, Weeks
1	Lichen planus	8	Severe	16
2	Eczematoid	6	Severe	14
3	Eczematoid	9	Severe	12
4	Exfoliative	5	Severe	16
5	Lichen planus	7	Moderate	8
6	Eczematoid	4	Moderate	4
7	Eczematoid	6	Moderate	4
8	Eczematoid	9	Moderate	6
9	Lichen planus	10	Moderate	5
10	Eczematoid	7	Moderate	6
11	Eczematoid	5	Moderate	7
12	Eczematoid	8	Moderate	8
13	Eczematoid	13	Moderate	3
14	Eczematoid	7	Moderate	4
15	Lichen planus	5	Moderate	9
16	Eczematoid	15	Mild	3
17	Eczematoid	6	Mild	5
18	Eczematoid	4	Mild	4
19	Lichen planus	9	Mild	4
20	Eczematoid	7	Mild	6
21	Eczematoid	9	Mild	2
22	Eczematoid	6	Mild	4

eruption was employed in this study. Direct examination of scrapings of the skin in a 10 per cent solution of potassium hydroxide and cultures were negative for pathogenic fungi in all cases. For all the patients in both groups roentgenologic studies of the small intestine were made with use of barium sulfate as a contrast medium in order to determine whether changes existed which might be related to a deficient absorption of food. In 8 of the 48 patients hypermotility was found, but in only 3 of these was it of sufficient degree to have possible pathologic significance. In view of the observations, the roentgenologic studies suggest that a deficient absorption of food did not play a major role in causing the disability.

All patients in both groups were observed to gain weight rapidly while receiving regular diets in the hospital. The cutaneous lesions began to disappear fairly rapidly, in most instances, regardless of

whether or not vitamin B complex was administered. However, a statistical analysis of the recovery rate in the two groups of patients disclosed that those with mild eruptions, receiving routine dermatologic care alone, recovered completely in an average of six weeks while the group receiving vitamin B complex plus routine dermatologic care recovered in an average of four weeks. The patients with moderate eruptions recovered in an average of eight weeks with only routine dermatologic care and in six weeks with the administration of vitamin B complex. Those with severe eruptions took on an average of twelve to sixteen weeks to recover, and the administration of vitamin B complex seemed to make little difference in the time of recovery. All patients except 2 with severe eruptions included in this study recovered completely and were returned to duty, which in most instances was permanent limited duty in the United States. Of the 2 who did not improve satisfactorily, 1 with a severe eczematoid type of eruption did recover after twelve months of continuous treatment. The other, with a severe lichen planus type of eruption, also recovered after twelve months of treatment.

COMMENT

There are a number of reports in the literature dealing with the relationship between vitamin B deficiency and dermatitis. Birch, György and Harris,[2] as well as Dann,[3] demonstrated that pyridoxine deficiency leads to the development of dermatitis in rats. Elvehjem, Madden, Strong and Woolley[4] showed that nicotinic acid is the anti-black-tongue and pellagra-preventive factor. Riboflavin is indispensable for human beings and animals alike, and its lack, according to Sebrell and Butler,[5] produces a typical dermatosis in human beings. So-called tropical avitaminosis, as stated by Wright,[6] is a polyavitaminosis manifested by a glazed, sore tongue, sore angles of the mouth, eczema of the anus, scrotum and vulva, rough keratotic skin of the extensor surfaces of the forearms and thighs, a glazed varnished condition of the canthi

2. Birch, T. W.; György, P., and Harris, L. J.: The Vitamin B_2 Complex: Differentiation of the Antiblacktongue and the "P.-P." Factors from Lactoflavin and Vitamin B_6 (So-Called "Rat Pellagra" Factor), Biochem. J. **29**:2830 (Dec.) 1935.

3. Dann, W. J.: The Vitamin G Complex: The Nonidentity of Rat Dermatitis Due to Vitamin B_6 Deficiency and the Dermatitis of Human Pellegra, J. Nutrition **11**:451 (May) 1936.

4. Elvehjem, C. A.; Madden, R. J.; Strong, F. M., and Woolley, D. W.: Relation of Nicotinic Acid and Nicotinic Acid Amide to Canine Black Tongue, J. Am. Chem. Soc. **39**:1767 (Sept.) 1939.

5. Sebrell, W. H., Jr., and Butler, R. E.: Riboflavin Deficiency in Man (Ariboflavinosis), Pub. Health Rep. **54**:2121 (Dec. 1) 1939.

6. Wright, E. J.: Polyavitaminosis and Asulphurosis, Brit. M. J. **2**:707 (Oct. 10) 1936.

and conjunctivitis. Gross [7] summarized the changes of the skin due to deficiency of vitamin B complex as being pellagra, ariboflavinosis, tropical avitaminosis and the Plummer-Vinson syndrome. He mentioned the fact that a number of different nonpellagrous cutaneous lesions respond to therapy with extract of liver, indicating that vitamin B deficiency may be a factor in their production. In group I of his series were the extensive scaling erythematous patches of dermatitis of unknown cause, which are associated with follicular keratosis and which resemble pityriasis rubra pilaris. In his group II, some patients with seborrheic dermatitis responded to liver by parenteral injection. In his group III were cases of vitamin B complex deficiency with moniliasis of the skin. In his group IV he included seborrheic dermatitis of the vulvoanal areas and kraurosis vulvae, which he stated may be due to a combined deficiency of vitamins A and B. His last group included the seborrheic exacerbation seen after arsphenamine therapy for patients with syphilis and disappearing with liver therapy.

The actual cause of lichenoid dermatitis is unknown. Quinacrine hydrochloride, used for malaria-suppressive therapy, has been considered as a causative factor.[8] Other contributing factors are also under consideration. Among them are (1) nutritional deficiency; (2) the moist warm tropical climate; (3) contact dermatitis; (4) unidentified bacteria, a virus or fungus, and (5) photosensitivity. The present study shows that vitamin B complex deficiency probably plays some role in the production of lichenoid dermatitis or that the presence of vitamin B complex deficiency may delay healing of the skin after the original dermatitis has developed. In view of the lack of fresh foods in the diet of the patients in New Guinea for many months, the decided loss of weight, the atypical character and distribution of the lesions, plus the accelerated recovery time of patients with moderate and mild eruptions when vitamin B complex is administered, it is our opinion that some degree of vitamin B complex deficiency is probably present. In most cases when the deficient vitamin is supplied to a person suffering from lichenoid dermatitis, the lesions improve more rapidly than when that person eats an adequate diet with fresh foods included but without supplemental vitamin B complex in large amounts. Whether vitamin B complex deficiency is a primary or a secondary factor in the production of New Guinea lichenoid dermatitis remains unsettled as yet, although it appears most probable that it is a secondary factor which tends to hinder recovery of the cutaneous lesions. Which portion of the

7. Gross, P.: Nonpellagrous Eruptions Due to Deficiency of Vitamin B Complex, Arch. Dermat. & Syph. **43**:540 (March) 1941.

8. Reactions Attributed to Atabrine, United States Army Subject Letter (SPMCB 441), Office of Surgeon General, July 19, 1945.

vitamin B complex is the essential agent remains to be determined by future investigation.

SUMMARY

Lichenoid dermatitis appeared among troops in the field who were subsisting on K or C rations without fresh foods for long periods and who had lost considerable weight. These troops had been taking quinacrine hydrochloride (atabrine) daily for months for the suppression of malaria. The disease begins on the dorsal surfaces of the extremities with erythema and vesicles, which may spread to involve other areas or even the entire body, in either an eczematoid or lichen planus type of eruption or a combination of both types of lesions. A severe exfoliative dermatitis may and often does supervene in any type of case. Two groups of patients were employed in our study. One group of 26 patients received routine dermatologic care alone and served as a control group. The other group, of 22 patients, received supplemental vitamin B complex both orally and parenterally in addition to routine dermatologic care. Vitamin B complex in large amounts caused a more rapid recovery when used in conjunction with routine dermatologic care for mild and moderate eruptions than the use of routine dermatologic care alone. Patients with severe eruptions recovered, but the time of recovery was not shortened by the vitamin B complex therapy. The cause of the lichenoid dermatitis is believed to be quinacrine hydrochloride; however, vitamin B complex deficiency probably plays a secondary role in the production of the disease or in its failure to heal rapidly once it appears.

CONCLUSIONS

1. The time of recovery from lichenoid dermatitis is shortened by the administration of vitamin B complex in large doses in addition to routine dematologic care. This improvement occurs in patients with moderate and mild eruptions but not in those with severe ones.

2. Vitamin B complex deficiency is a factor, probably secondary, in causing lichenoid dermatitis.

3. The fraction or fractions of the vitamin B complex group which are responsible for the more rapid recovery are yet to be determined.

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PROGRESSIVE RECURRENT DERMATOFIBROMA (DARIER-FERRAND)

Anatomoclinical Study

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AS OFTEN happens in dermatology, to the confusion of those who are beginning the study of this specialty, the cutaneous disease which I shall discuss in this paper is known by a large number of names. In Germany, for instance, it has been called fibrosarcoma (Virchow), fusocellular fibrosarcoma (Unna), fibroblastic sarcoma or sarcomatous fibroma (Zurhelle) and tuberous or protuberant fibrosarcoma or dermatofibrosarcoma (Hoffmann). In France it is described as progressive and recidivous dermatofibroma of Darier and Ferrand and fibrosarcoma of the skin.[1] Hertzler[2] has also described this disease under the name of sarcoma of the skin. These tumors have been described by Bezecny[3] as dermatofibrosis protuberans et progrediens. McMaster[4] has named them sarcomatoid fibroma of the skin, and Mosto[5] has called them neuroma or dermatoschwannoma.

DEFINITION

According to Woringer,[6] progressive and recurring dermatofibromas are fibrous tumors of neoplastic evolution which develop on a fibrous plaque that in most cases begins several years earlier and is localized at the level of the abdominal wall. Its evolution is

1. Favre, M., and Josserand, A.: Les fibrosarcomes de la peau, in Darier, J., and others: Nouvelle pratique dermatologique, Paris, Masson & Cie, 1936, pt. 6, pp. 824-836.

2. Hertzler, A. E.: Fibrosarcomatous Tumours of the Skin of the Trunk, Characterised by Attenuated Dermal Surfaces, Ann. Surg. **84**:489-496, 1926.

3. Bezecny, R.: Dermatofibromatosis Protuberans et Progrediens, Arch. f. Dermat. u. Syph. **162**:782-791, 1930.

4. McMaster, P. E.: Sarcomatoid Fibroma of the Skin (Progressive and Recurring Dermatofibroma), Ann. Surg. **99**:338-347, 1934.

5. Mosto, D.: Dermatoneurome, Ann. de dermat. et syph. **10**:845-851, 1929; Sobre una nueva interpretacíon de los dermatofibromas de Darier, Semana méd. **1**:855-859, 1929.

6. Woringer, F.: Dermatofibromes progressifs et récidivants, in Darier, J., and others: Nouvelle pratique dermatologique, Paris, Masson & Cie, 1936, pt. 6, pp. 573-580.

progressive and extensive, and it is refractory to treatment. In spite of this, such tumors show only local malignant changes and do not give rise to metastases. It should be noted that progressive and recurring dermatofibromas, according to the observations of some authors, may give rise to cutaneous or internal metastases and that the initial phase is not always characterized by the classic fibrous plaque. Fidanza [7] has defined these tumors as lesions which, from the clinical point of view, are characterized by neoplasm of the skin whose objective aspect is peculiar and whose evolution is progressive and indefinite; according to him such tumors are refractory to treatment and show a strong tendency to recurrence after removal, denoting a certain amount of local malignant characteristics; they occur preferentially in the abdominal wall and inguinal regions.

HISTORICAL OUTLINE

The history can be divided into two stages. The first stage ends in 1924 with the appearance of the masterly paper of Darier and Ferrand [8]; the second is the stage which continues up to the present. The first phase is somewhat confused, for the problem had not yet been studied as a whole and in detail. According to Binkley,[9] Sherwell [10] in 1890 presented to the New York Dermatological Society a case for diagnosis and suggested that it was one of hypertrophic leprosy; a photograph of the patient was published in Piffard's book, but the case presents all the aspects of progressive and recurring dermatofibroma. In 1901 Johnston,[11] in a paper read before the Academy of Medicine of Buffalo and the American Dermatological Association, referred to a case in which he diagnosed the disease as myxosarcoma on account of the myxomatous degeneration which it showed. Later in 1903, Johnston [12] diagnosed the disease in his case as fibrosarcoma cutis and reported another typical case. In 1890 Taylor [13] reported a case. In 1904 Kartscher and Pfeiffer [14] reported cases in which they

7. Fidanza, E. P.; Carrillo, F., and Ocana, T.: Dermatofibromas progressivos e recidivantes de Darier, Rev. argent. dermatosif. **19**:26-45, 1935.

8. Darier, J., and Ferrand, M.: Dermatofibromes progressifs et récidivants ou fibrosarcomes de la peau, Ann. de dermat. et syph. **5**:545-570, 1924.

9. Binkley, G. W.: Dermatofibrosarcoma Protuberans, Arch. Dermat. & Syph. **40**:578-594 (Oct.) 1939.

10. Sherwell, S.: Morphea, J. Cutan. & Genito-Urin. Dis. **8**:72, 1890.

11. Johnston, J. C.: Sarcoma and the Sarcoid Growths of the Skin, J. Cuta. & Genito-Urin. Dis. **19**:305-325, 1901.

12. Johnston, J. C.: Fibrosarcoma Cutis, J. Cutan. & Genito-Urin. Dis. **21**:23-26, 1903.

13. Taylor, R. W.: Sarcomatous Tumours Resembling in Some Respects Keloid, J. Cutan. & Genito-Urin. Dis. **8**:384-387, 1890.

14. Kartscher and Pfeiffer, cited by Hoffmann.[16]

made the diagnosis of desmoid, and this fact led Scomazzoni [15] and McMaster [4] to believe that these cases were the first reported in the literature on the subject. Hoffmann [16] disagreed with this assumption. Senear, Andrews and Willis,[17] basing their arguments on Hoffmann's work, affirmed that Coenen [18] was the first to describe progressive and recurring dermatofibromas, in 1909. Favre and Josserand,[1] however, stated that the disease was known to Unna [19] in 1894. But on Nov. 8, 1923, at a meeting of the French Society of Dermatology and Syphilography, Rabut and Cailliau [20] showed a case of fibroma of the abdominal wall. Darier [21] commented on this case, pointing out its importance and stating that he had already seen 2 cases. In 1924 Darier and Ferrand [8] made a study of 4 cases, 2 hitherto unpublished, 1 of Rabut and Cailliau [20] and 1 published on Feb. 14, 1924. This was one of the most complete studies ever made of the subject, and the authors suggested for the morbid condition the name of progressive and recurring dermatofibroma or fibrosarcoma of the skin. Darier and Ferrand [8] expressed the belief that this new morbid entity had not yet been mentioned in the nosography of the subject. In strict justice to Darier and Ferrand it should be mentioned that it was only after their masterly and detailed description that this neoplasm became really known, as is shown by the greater number of cases published after 1924.

In 1925 Hoffmann,[16] in Germany, mentioned 3 cases and made a general review of the literature. He came to the conclusion that this disease was really first described in world medical literature by Coenen [18] in 1909 and that Kuznitzky and Grabisch [22] also wrote on the subject in 1921. Hoffmann [16] managed to get together 15 cases, including his own, reported in world medical literature up to the

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15. Scomazzoni, T.: Contributo alla clinica e alla histologia dei fibrosarcomi cutanei, Gior. ital. di dermat. e sif. **67**:115-135, 1926.

16. Hoffmann, E.: Ueber das knollentreibende Fibrosarkom der Haut, Dermat. Ztschr. **43**:1-28, 1925.

17. Senear, F. E.; Andrews, E., and Willis, D. A.: Progressive and Recurrent Dermatofibrosarcoma (Dermatofibrosarcoma Protuberans), Arch. Dermat. & Syph. **17**:821-832 (June) 1928.

18. Coenen, H.: Granulationsgeschwülste und Sarkome, Beitr. z. klin. Chir. **63**:337-346, 1909.

19. Unna, P. G.: Die Histopathologie der Hautkrankheiten, Berlin, A. Hirschwald, 1894; The Histopathology of the Diseases of the Skin, translated by N. Walker, New York, The Macmillan Company, 1896.

20. Rabut, R., and Cailliau: Fibrome de la paroi abdominale, Bull. Soc. franç. de dermat. et syph. **30**:392, 1923.

21. Darier, J., in discussion on Rabut and Cailliau.[20]

22. Kuznitzky, E., and Grabisch, A.: Ueber myxomatöse Fibrosarkome der vorderen Brustwand, Arch. f. Dermat. u. Syph. **131**:23-32, 1921.

date of the publication of his paper in 1925. He also mentioned 6 other cases of tumors described in the literature on the subject as desmoid but which he presumed to be progressive recurring dermatofibroma. Senear, Andrews and Willis,[17] however, preferred not to take these cases into consideration in view of the deficiency of data and the uncertainty as to the true diagnosis. After the original paper of Darier and Ferrand,[8] in France, cases were reported by Touraine and Aubrun [23]; Gaté, Ricard, Guilleret and Moreau [24]; Chatelier [25]; Touraine and Payet [26] Margarot, Plagniol and Guibert [27]; Darier [28]; Milian and Périn [29]; Pautrier and Woringer,[30] and Weissenbach, Thibaut, Martineau and Bouwens.[31] In Italy cases have been reported by Scolari,[32] Scomazzoni,[15] Levi,[33] Pinetti,[34] Bertaccini [35] and Casazza.[36] In the United States cases have been reported by Senear, Andrews and Willis [17]; Weidman [37]; Binkley [9]; McMaster [4]; Michelson [38]; Taylor,[13]

23. Touraine, A., and Aubrun, W.: Fibrosarcome tubéreux de la peau de l'abdomen, Bull. Soc. franç. de dermat. et syph. **40**:1689-1690, 1933.

24. Gaté, J.; Ricard, A.; Guilleret, P., and Moreau, P.: Un cas de fibrosarcome de la peau, Bull. Soc. franç. de dermat. et syph. **45**:162-165, 1938.

25. Chatelier, M. L.: Trois nouveaux cas de dermatofibromes tubereux de la peau, Bull. Soc. franç. de dermat. et syph. **37**:608-610, 1930.

26. Touraine, A., and Payet, M.: Fibro-sarcome tubéreux de l'abdomen, Bull. Soc. franç. de dermat. et syph. **45**:1675-1677, 1938.

27. Margarot, J.; Plagniol, P., and Guibert, H. L.: Dermatofibromes progressifs et récidivants (fibrosarcomes) de la paroi abdominale, Bull. Soc. franç. de dermat. et syph. **38**:1156-1164, 1931.

28. Darier, J.: Un nouveau cas de fibrosarcomes de la peau, opéré et guéri, Bull. Soc. franç. de dermat. et syph. **33**:32-36, 1926.

29. Milian, G., and Périn, L.: Fibro-sarcome au début de la région malléolaire interne, Bull. Soc. franç. de dermat. et syph. **33**:621-623, 1926.

30. Pautrier, L. M., and Woringer, F.: Dermato-fibrome progressif et récidivant de Darier-Ferrand, Bull. Soc. franç. de dermat. et syph. **41**:611-617, 1934.

31. Weissenbach, R. J.; Thibaut, D.; Martineau, J., and Bouwens, G.: Tumeures cutanées extensives de la région épigastrique évoluant depuis 25 ans (fibromes ou fibrosarcomes), Bull. Soc. franç. de dermat. et syph. **45**:934-937, 1938.

32. Scolari, E. G.: Del fibrosarcoma cutaneo, Gior. ital. di dermat. e sif. **71**:1533-1558, 1930.

33. Levi, I.: Sopra un caso di fibrosarcoma primitivo delle cute del pene, Gior. ital. di dermat. e sif. **71**:1559-1574, 1930.

34. Pinetti, P.: Su di un caso di dermatofibroma progressivo recidivante di Darier a sede ed a struttura istopatologica non commune, Gior. ital. di dermat. e sif. **73**:811-820, 1932.

35. Bertaccini, G.: Fibro-sarcoma cutaneo primitivo in un bambino de cinque anni, Arch. ital. di dermat., sif. **1**:1-9, 1925.

36. Casazza, R.: Osservazioni su un gruppo di non comuni casi di oncologia dermatologica, Arch. ital. di dermat., sif. **8**:3-118, 1932.

37. Weidman, F. D.: Fibrosarcoma (?) of the Thigh, Arch. Dermat. & Syph. **5**:421-422 (March) 1922.

(Footnotes continued on next page)

and others. In Canada only 2 cases have been reported—by Usher.[39] In Argentina cases have been reported by Fidanza, Carrillo and Ocana [7]; Fernández Blanco [40]; Alejandro and Bosq [41]; Puente and Copello,[42] and Seminario and Pessano.[43] In 1928 Kiess [44] observed another case and managed to get together 26 others already reported in world literature. Volk,[45] in 1928, in Vienna, and Nicolau,[46] in 1929 in Bucharest, reported 1 case each. In Brazil I have found records of only 1 published case, that of Fraga,[47] and accordingly, I believe mine to be the second case reported in this country. The diversity of opinion among different authors as to the chronologic order of the first cases published is due to the confusion which existed in the early stages resulting from insufficient and unsatisfactory clinical and histologic description and also from variations of nomenclature. Darier, Ferrand and Hoffmann corrected these deficiencies, giving to these interesting tumors a definite place in human pathology.

CLASSIFICATION

Before beginning the clinical description, it is indispensable to undertake the classification of these growths among the cutaneous tumors. As is known, the connective tissue is derived from the embryonic mesenchyma. In spite of the fact that this tissue is widely diffused in the organism, fibromas, with rare exceptions, are found only in the derma (dermatofibromas), the sheath of the musculus rectus abdominis (desmoid), the periosteum at the base of the cranium

38. Michelson, H. E.: Dermatofibrosarcoma Protuberans, Arch. Dermat. & Syph. **25**:1127 (June) 1932.

39. Usher, B.: Progressive and Recurrent Dermatofibrosarcoma (Dermatofibrosarcoma Protuberans), Brit. J. Dermat. **41**:363-369, 1929.

40. Fernández Blanco, M.: Consideraciones acerca de la histopatogenia de la enfermidad de Recklinghausen, Semana méd. **2**:982-987, 1929.

41. Alejandro, S., and Bosq, P. J.: Dermatofibroma de Darier, Rev. argent. dermatosif. **22**:698-699, 1938.

42. Puente, J. J., and Copello, C.: Dermatofibromas en la pared abdominal, Rev. argent dermatosif. **12**:152, 1927; Dermatofibroma en la pared abdominal Prensa med. argent. **14**:575, 1927.

43. Seminario, C., and Pessano, J.: Los dermatofibromas de Darier y Ferrand son formas frustradas de la enfermidad de Recklinghausen? Rev. argent. dermatosif. **14**:61-69, 1930.

44. Kiess, O.: Ein neuer Fall von Dermatofibrome progressif oder Fibrosarcome, Dermat. Wchnschr. **86**:1-7, 1928.

45. Volk: Fibrosarkom, Dermat. Wchnschr. **87**:1809, 1928.

46. Nicolau, S.: Fibrosarkom der Bauchgegend, Dermat. Wchnschr. **89**:1342, 1929.

47. Fraga, A.: Dermatofibromas progressivose recidivantes, An. brasil. de dermat. sif. **4**:69-71, 1933.

and of the long bones (basal and parosteal fibromas) and the ovarian stroma (ovarian fibromas). Of all these varieties the only ones that are of interest among those which occur in the derma are the progressive and recurring dermatofibromas which are connective neoplasms with a special clinical picture. Writers on the subject differ in their classification of these tumors as malignant or benign. This divergence of opinion is understandable, for it is not always easy to determine whether or not a cutaneous tumor is malignant. The histologic structure alone is not sufficient in all cases to determine malignancy, for the clinical behavior of the tumors is also of great importance. Eller [48] stated that progressive recurring dermatofibromas belong to the class of malignant tumors originating in the connective tissue. To the same group belong fibrosarcomas, myxosarcomas and liposarcomas, which constitute a variety of fibrosarcoma with a special clinical picture. Woringer [6] included them in the group of benign connective fibrocytic and histiocytic tumors along with the pastille fibroma of Civatte, the keloids and the muscular dissociating fibroma of the abdominal wall (desmoid), of the myxomas and of the histiocytomas. Favre and Josserand [1] included them among the malignant connective tissue tumors along with the other cutaneous sarcomas. As will be seen in the succeeding pages, progressive recurring dermatofibromas are really tumors which by their clinical and histologic characters may belong either to the malignant or to the benign group of connective tissue neoplasms. Hence, in the classic examples of the growths one meets with characteristics which lead one to put them among the malignant connective tissue tumors; such a characteristic, for example, are resistance to treatment, tendency to recurrence and histologic features. But the elements which favor their nonmalignancy are the absence of any effect on the general health, the absence of metastasis in most cases and their slow evolution. It is to be concluded therefore that these tumors, by their clinical and histologic characters, partake of the nature of both the malignant and the benign tumors, on the borderline of both. The criterion for judging whether or not such tumors are malignant is variable, because they show manifestations peculiar to both malignant and benign neoplasms, constituting a link between them and oscillating toward one side or the other as shown by the clinical cases so far observed. Bezecny [3] stated the belief that cutaneous fibrosarcoma is a diffuse fibromatosis due to hereditary predisposition which in its development gives rise to tumors. I am of the opinion that the hereditary factor does not seem to exercise any influence, for up to the present no case of familial involvement has been reported and most authors are of the same opinion.

48. Eller, J. J.: Tumors of the Skin, Philadelphia, Lea & Febiger, 1939, p. 437.

Binkley,[9] after studying 6 cases, expressed the idea that dermatofibrosarcoma, in spite of having definite clinical characteristics, is not different histologically from the other fibrosarcomas. Fidanza[7] asserted that, in his case at least, the growth was a fibroma, since no polymorphism, poikilochromia or cellular monstrosities were observed. He could not, however affirm that this tissue may not be transformed partially or totally into a sarcoma under influences which cannot be exactly defined. Fernández Blanco,[40] in describing a case of cutaneous fibrosarcoma localized in the left inguinal region which began in infancy, expressed the belief that his patient, although not suffering from von Recklinghausen's disease, showed formations whose histologic features are those of the neurinomas encountered in this disease. This discovery made the author wonder whether he was not face to face with a case of abortive recurring von Recklinghausen's disease localized strictly in one region of the body. Seminario and Pessano,[48] also writing about a clinical case, wondered whether what is described as progressive recurring dermatofibroma or fibrosarcoma is not really an abortive form of von Recklinghausen's disease in process of transformation into sarcoma. Bobbio[49] affirmed that, according to his researches, dermatofibroma should be classified between desmoids and keloids, on the one side, and between the fibromas and fibrosarcomas, on the other.

DESCRIPTION

The symptoms of progressive recurring dermatofibromas are, with few exceptions, typical. The favorite sites are the abdomen and the inguinocrural region. The authors, though, can find no explanation for this preference except the histogenic theory of Binkley.[9] The localization of protuberant dermatofibrosarcomas, however, is not confined to the abdomen and inguinocrural regions but may be on any part of the cutaneous tegument (fig. 1). Thus, they have been observed on the back, deltoid region, thighs, shoulders, dorsum of the foot, gluteal region, region of the kneecap, penis, malleolar region, wrist, face, submammary region, hairy scalp, etc. Localization on the head is rare, for up to the present only 4 cases with such localization have been reported: 2 on the hairy scalp and 2 on the face. In the former 2 cases, the sites of localization were the occipital region and the forehead and vertex. The tumor localized in the occipital region was observed by Yamasaki,[50] in Japan, and the one on the vertex and forehead was observed by me, in Brazil. The latter was the fourth one mentioned in world literature localized on the cephalic segment

49. Bobbio, A.: Tre casi de dermatofibroma, Cancro **2**:186-193, 1931.

50. Yamasaki, I.: Zur Kenntnis des Dermatofibrosarcoma protuberans (E. Hoffmann), Jap. J. Dermat. & Urol. **43**:44-48, 1938.

and the second on the hairy scalp; it can thus be deduced that this localization is extremely rare. My case, indeed, is very similar to that of Yamasaki.[50] In typical cases of dermatofibrosarcoma the tumors are nearly always multiple, but single ones have been observed.

The shape of the tumor is variable—spherical, fungiform, pyriform, sessile, pedunculated, lobular, etc. The size varies from that of a peanut up to that of the head of a fetus. As regards the dimensions of the one in my case, I verified that it was one of the largest yet reported. The outlines or limits are always well defined, and the color varies; it may be violet red, pink or reddish. The surface may be smooth and uniform or eroded. When the surface of the tumor becomes eroded, it may turn red like a tomato and acquire a vegetative appearance. The excrescences are generally hard and cartilaginous but may become soft, especially when the surface becomes eroded. No liquid or secretory products are observed in the lesion, except when the surface becomes ulcerated. In most cases no changes in sensibility are observed. Involvement of lymph nodes has been reported in some cases but is not the rule; the enlargement must be regarded as being due to secondary infection and not to the tumor process itself. It is true that in the case of Levi [83] there was lymphatic metastasis, but this is the exception and not the general rule. It is well to emphasize at this point that progressive and recurring dermatofibroma, as described by Darier and Ferrand, presents a group of symptoms so typical and peculiar that certain cases, as I found in reviewing the world literature on the subject, differ so greatly from those described by the aforementioned authors that one is left in doubt as to the true diagnosis.

The evolution of a typical dermatofibrosarcoma takes place in two stages; the first of these consists of the formation of a fibrous plaque and the second is represented by the appearance of a tumor formation in this plaque. The period which elapses between stage one and stage two varies from case to case. The fibrous plaque may appear as such from the start or may be preceded by the appearance in the hypodermis of small hard infiltrating nodules which increase slowly in size and number and coalesce to form a pseudokeloid or sclerodermiform plaque which varies in size and may attain the dimensions of one's palm. The surface of the plaque is smooth, and pale rose or dark in color and is hard to the touch, and the skin over it cannot be folded. The plaque is not attached to the subjacent tissues and can be made to slide over them. There are no subjective symptoms at this stage, and the disease must not be confused with scleroderma. Some time, generally some years, after the plaque is fully formed, the tumor elements appear, and the last ones to form may attain an uncommonly large size in contrast with the slow growth of those which appear first. This is exactly what happened

in my case, in which the first tumors grew more slowly than the subsequent ones and much more so than those most recently formed.

The description just given applies to the typical cases, but there are atypical ones. In Casazza's case,[36] for example, there was a limited zone of adherence to the deeper tissues. At times the surface of the plaque is not smooth but is studded with nodules, some of which are perceptible only on palpation while others are raised above the surface. In certain cases there is no stage of fibrous plaque formation; the disease begins with the appearance of one or more tumors. It is exactly those cases which differ from the classical clinical picture that need to be analyzed minutely both from the clinical point of view and from the histopathologic aspect in order to be classified with precision. In one of Fessler's [51] cases, for example, the clinical aspect of the fibrosarcoma was that of a fibroma, but the histologic examination showed transitional forms between fibroma and fusocellular sarcoma. Some cases, like the one reported by Nastase and Ionescu,[52] although conforming closely to the classical description of Darier and Ferrand, differ from it histologically by the presence of giant cells indicating a growth more malignant than fibrosarcoma. The neoplasm is restricted to the skin and hypodermis, but in some cases invasion of the underlying muscle has been observed. Lapa [53] affirmed that these tumors never ulcerate and stated that up to the time when his paper was written the appearance or spontaneous existence of this complication had never occurred. But in my case and in others there was ulceration. In some cases of fibrosarcoma the tumors are associated with other morbid manifestations, but this fact has no special pathologic importance. In the third case reported by Darier, for example, the cutaneous neoplasm was accompanied with a uterine fibroma. In the majority of cases pain is not mentioned as a symptom, but Senear [17] and Hoffmann [16] reported slight pain in some of the cases studied by them. Hemorrhage may supervene during the evolution of the tumors, and at the end there may be gangrene.

The question of the malignancy of these tumors is one that needs some attention. This question should be looked at from two points of view, the clinical and the histologic. From the former, fibrosarcoma behaves like a malignant tumor in that it is progressive, recurs when incompletely excised and can give rise to internal or cutaneous metastases. In most cases the evolution of the disease is slow. The tumors may remain stationary for a long time and then, later, without apparent cause

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51. Fessler, A.: Ein Fall von Dermatofibrosarcoma protuberans, Dermat. Ztschr. **72**:221-226, 1935.

52. Nastase, G., and Ionescu, E. I.: Fibro-sacrome ou dermatofibrome des cellules atypiques, Bull. Soc. franç. de dermat. et syph. **43**:1529-1536, 1936.

53. Lapa, A.: Dermato-fibromas progressivos e recidivantes ou dermato-fibrosarcoma protuberans, Lisboa méd. **6**:355-376, 1929.

or as a result of traumatism, begin to grow rapidly. The duration of the disease also varies from case to case; cases have been observed in which the disease lasted for fifteen, thirty-eight, forty-five and even as long as sixty years. No case of malignant sarcomatous change has yet been reported, except that of Alkiewicz.[54] Death generally occurs from some local or general intercurrent cause. Different authors have held different ideas about the possibility of the occurrence of metastasis. Darier [8] observed 1 case in which there appeared a cutaneous tumor far from the primary focus, but he stated that internal metastases are doubtful. Darier and Ferrand [8] expressed the belief that remote cutaneous metastases occur through the blood stream or at least the lymphatic channels. Usher [39] said that in his opinion the dissemination takes place by lymphatic channels but denied the existence of metastases to lymph nodes, which were observed by Levi.[33] Although internal metastases were reported by Bezecny,[55] Renzo,[56] Sciacchitano [57] and Binkley,[9] they are rare. The frequency of progressive recurring dermatofibroma is differently considered by different authors. Pinetti [34] in 1932 mentioned 40 cases reported; McMaster [4] in 1931 mentioned 39, and Ruiter [58] in 1934 cited 37. Woringer [6] in 1936 said that the disease was rare because up to that time only 35 cases had been reported in world medical literature. In 1938 Touraine and Payet [26] spoke of 50 published cases. Hertzler [2] reported 22 cases observed during twenty-five years of practice, but McMaster expressed the opinion that these tumors cannot be considered examples of progressive recurring dermatofibroma because they were capsulated and gave rise to metastases. Beck [59] in 1938 managed to catalogue 62 cases reported in world literature. In my search of the bibliography reviewing the subject, I found that 124 cases had been registered up to 1943, and of these I obtained the clinical summaries of 111. Sutton and Sutton [60]

54. Alkiewicz, J.: Sur les rapports entre l'hystiocytome et le dermatofibrome de Darier-Ferrand, Rev. franç. de dermat. et de vénéréol. **15**:195-210, 1939.

55. Bezecny, R.: Lungenmetastasen beim Dermatofibrosarcoma protuberans, Arch. f. Dermat. u. Syph. **169**:347-353, 1933.

56. Renzo, cited by Favre and Josserand.[1]

57. Sciacchitano, G.: Sopra un caso di fibro-sarcoma cutaneo con metastasi polmonari, Tumori **9**:427-438, 1935.

58. Ruiter, M.: Zwei Fälle von progressiven und rezidivierenden Fibrosarcomen der Haut (Dermatofibrosarcoma protuberans), Acta dermat.-venereol. **17**: 162-170, 1936; Dermatofibrosarcoma protuberans, Nederl. tijdschr. v. geneesk. **79**:4415, 1935.

59. Beck, C. H.: Zur Kenntnis des Dermatofibrosarcoma protuberans, Arch. f. Dermat. u. Syph. **178**:260-268, 1938.

60. Sutton, R. L., and Sutton, R. L., Jr.: Diseases of the Skin, ed. 10, St. Louis, C. V. Mosby Company, 1939, p. 775.

stated that Geschickter and Lewis [61] observed 8 cases, in 7 of which the patients were women. Geschickter and Lewis' cases [61] were of simple dermatofibroma and not of protuberant dermatofibrosarcoma.

Summarizing his conclusions, Beck [59] stated that a case of dermatofibrosarcoma was described, the patient being a woman of 54 and the tumor being situated in the abdomen. The morbid picture of dermatofibrosarcoma protuberans was completed from the data of 63 cases described. In this way the following conclusions were derived:

1. This disease occurs with the same frequency in the two sexes.

2. The favorite sites of the disease are the abdomen, thorax, lower limbs, back, inguinal fold and upper limbs.

3. In 75 per cent of cases the tumor had already existed for five years before the beginning of treatment, while in 19 per cent the disease had existed for twenty-six years or more.

4. The first manifestations occurred in a small percentage of cases before the patient's twenty-sixth birthday, while in 11 per cent these first symptoms appeared before the age of 6. In more than half the cases treatment was begun between the ages of 36 and 55.

5. Dermatofibrosarcoma protuberans of the thorax shows a greater tendency to myxomatous degeneration than that on any other part of the body.

6. The older the tumor, the more frequent the occurrence of myxomatous degeneration is.

7. It is not yet possible to form an idea of the possible malignancy of a dermatofibrosarcoma either by its age or by its histologic structure, although hitherto more signs of malignancy have been discovered in cases with myxomatous degeneration than in others.

8. It is probable that, in spite of all, the tumors described by Hertzler are examples of dermatofibrosarcoma protuberans.

RACES

Dermatofibrosarcoma has been found in nearly all races: the white, the yellow and the black. My case and that of Fraga [47] constitute the first ones reported in world literature as occurring in brown mestizos (mulattoes). The largest number of cases have occurred among white persons, followed by black persons, Asiatics and mestizos in that order.

SUBSIDIARY TESTS

The laboratory diagnosis of progressive recurring dermatofibrosarcoma rests on the anatomicopathologic examination. For this purpose fragments for biopsy are taken in accordance with the rules already

61. Geschickter, C. F., and Lewis, D.: Tumors of Connective Tissue, Am. J. Cancer **25**:630-655, 1935.

laid down for this purpose. It is advisable, however, that they be taken from various parts of the tumor elements so as to obtain specimens of the various evolutionary phases, that is to say, different structural aspects, as happens in certain cases. Some authors have reported positive Wassermann reactions in certain cases, but this shows only that the patients were suffering from syphilis and not that their respective cutaneous lesions were of syphilitic origin; this is borne out by the inefficacy of syphilitic treatment in these cases. My case constituted a good example of this for the Wassermann reaction was positive but antisyphilitic treatment had no influence on the course of the cutaneous lesions.

PATHOLOGIC ANATOMY

I shall divide the pathologic anatomy into two parts: one part dealing with the structural changes found by various authors and the other the study of the preparations obtained by me in the case which is dealt with in this paper. Generally speaking, the pathologic anatomy of progressive recurring dermatofibrosarcoma is not very different from that given in the classic description of Darier and Ferrand,[8] but there are circumstances in which some abnormality occurs. Pautrier and Woringer [62] found, in 1 case, small nerves and isolated nerve filaments running through the interior of fibromatous bundles. However, sections made in series and the topographic layout showed that these were nerve endings around a hair follicle which had already disappeared as well as of remains of nerves which had resisted the destructive action of the tumor substance. Fatty infiltration and myxomatous degeneration have already been mentioned. It has been found that old tumors are more fibrous and the more recent ones are richer in cells. The capsule found by Hertzler [2] in his cases has not been mentioned by the majority of authors who have studied the subject. Favre and Josserand,[1] however, stated that some authors refer to a well defined capsule but affirm that the presence of such elements is not important, since capsulated fibrosarcomas have already been observed. According to Favre and Josserand,[1] the differentiated skin structures, such as nerves, glands and hair, disappear on account of the infiltration, but there have been cases in which the smooth muscles remain intact and in which the sweat glands persist, dissociated or encysted. Atypical cellular and karyokinetic forms have been observed. Margarot [27] and Pinetti [34] observed cases in which the vascular formations were so well developed that it was possible to refer to the tumors as angiofibromas and angiosarcomas. Besides such changes, there are also mentioned necrotic areas, sclerosis of the vascular walls and oblitera-

62. Pautrier, L. M., and Woringer, F.: Dermat-fibrome de Darier-Ferrand, Bull. Soc. franç. de dermat. et syph. **44**:2171-2174, 1937.

tion of the lumen of the blood vessels by endovascular proliferation. As regards my case, I selected for biopsy three fragments of tumors in different stages of evolution. I shall, however, describe only one of these and make a general interpretation of the histologic changes met with in all three. The histologic description of my preparations is as follows:

SPECIMEN 1.—The whole surface of the preparation was ulcerated, showing a relatively extensive area covered with a fibrinopurulent exudate, the superficial layers of which were infiltrated by polymorphonuclear neutrophils, plasma cells and lymphocytes, one or other of these inflammatory cells predominating according to the area. It must be borne in mind also that the vascularization is distinctly more pronounced in the upper than in the deep layers, there being present in the superficial layers numerous new blood vessels some of them showing dilatation of their lumen. This superficial zone is therefore represented by true granulation tissue. Below this granulation tissue and prolonging it insensibly, there is a connective tissue neoplasm fasciculated in structure (fig. 1 *A*), with bands of tissue crossing each other in the most varied manner, now transversally, now obliquely and even at times in a kind of whorl. As regards cytology, the tumor is found to consist of fusiform cells, with nuclei of varying size, some being long and thin and others shorter and thicker; the former are more hyperchromatic than the latter. These nuclei generally contain one or two nucleoli, and the protoplasm has indistinct borders. A fibrillary intercellular substance is distinctly visible (fig. 1 *B*). When stained by Van Gieson's method these fibrillae do not stain with fuchsin, but with Mallory's stain for collagen they are stained blue. There are no elastic fibers (Rubens Duval method). No karyokinetic figures were found, but a small number of atypical cells were met. The majority of the blood vessels are lined only with endothelium. In some of them, however, the other lining tissues are met. There is neither myxomatous degeneration nor fatty infiltration.

INTERPRETATION OF THE HISTOLOGIC CHANGES

According to Moacir Junquiera, the histologic changes in the specimens which were taken at the levels of the different tumors showed that the structure of the tumors was about the same, for all of them were connective tissue neoplasms consisting of strands which crossed each other in different directions and which were built up of elongated cells that showed practically no pleomorphism, apart from a few atypical forms, which were not seen, however, in all of the blastomas. The absence in all of them of karyokinesis, either typical or atypical, must be emphasized. In some preparations the dividing line between the neoplasm and the superficial derma could be observed, but no capsular formation was to be seen. Only one of the tumors was ulcerated, but in the parenchyma itself in no case was there observed any necrotic area or any form of degenerative change. From all these facts, it can be concluded that I was really dealing with cases of dermatofibroma because no elements were met indicating evident histologic malignancy;

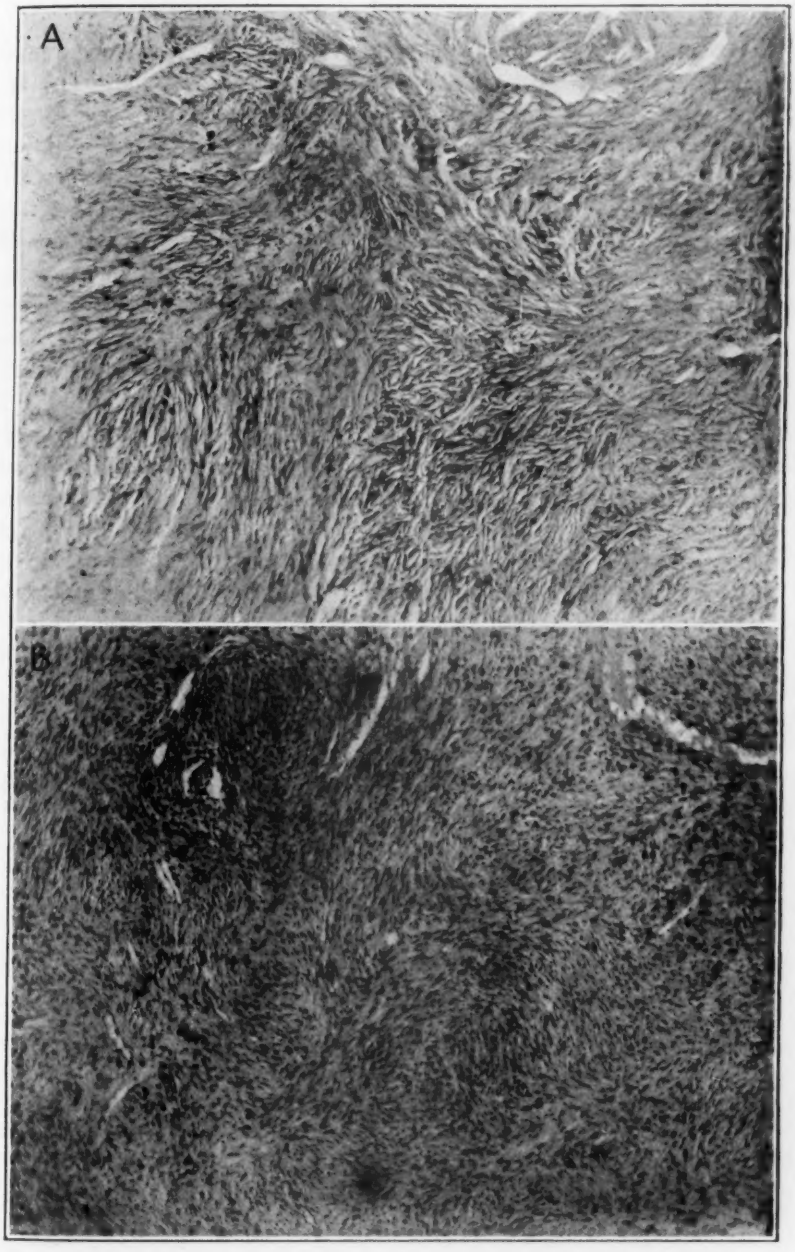

Fig. 1.—*A*, section showing the fasciculated structure and the varied direction of the connective tissue strands. *B*, preparation showing the greater abundance of the intercellular collagen.

there were therefore no grounds for classifying the tumors as fibrosarcomas or fibroblastic sarcomas.

It must be borne in mind, however, that, as can be deduced from the histologic description of the cases of different authors, these neoplasms do not present a characteristic and unchanging histopathologic structure; this on the contrary varies according to circumstances. The final diagnosis, therefore, must be based rather on the clinical symptoms than on the laboratory examination. The histologic examination serves as a complement to the clinical examination.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis must be made between this disease and benign connective tissue fibrocytic or histiocytic tumors, malignant connective tissue tumors, von Recklinghausen's disease, simple pedunculated fibroma and patchy scleroderma. Among benign fibrocytic connective tissue neoplasms are included fibromatoses and fibromas properly so-called. In my case chiefly and in that of Yamasaki,[50] on account of the exceptional localization on the hairy scalp, it is necessary in making the differential diagnosis to bear in mind the possibility of confusion with the wens of this region and with the cylindromas, which are tumors called by the English "turban tumors"; many illustrative cases of these are to be found in the excellent work of Ronchese.[63]

HISTOGENIC THEORIES

Various theories have been formulated to explain the histogenesis. Binkley [9] stated:

> Because of the unusual predilection of dermatofibrosarcoma for the anterior surface of the body to the right and left of the midline, a possible embryologic relation to the mammary ridge suggested itself. To test this theory, a spot map (fig. 2) was made showing the situations of the tumors thus far reported. This showed at once that these tumors occur with remarkable frequency at or near the mammary ridge. Many of them are situated on the neck, above the clavicle, and also on the upper part of the chest above or below the breast. On the abdominal wall, they are usually in the lower quadrants several centimeters to the right or left of the umbilicus. The growths occur frequently in the groin and occasionally on the medial side of the superior portion of the thigh. A few tumors have been observed on the back, on the buttocks and on the extremities, and one was on the penis.
>
> Wiedersheim, along with other embryologists, has stated that "in the great group of Carnivora and in the pigs, the teats are arranged in two rows converging toward the pelvic region." Pinkus stated that "the mammary ridge in young embryos is sometimes seen extending over the dorsum and down to the caudal region." This fact would explain the situation of some tumors on the back or

63. Ronchese, F.: Multiple Benign Epithelioma of the Scalp (Turban Tumors), Am. J. Cancer **18**:875-887, 1933.

on the buttocks, usually a few centimeters to the right or left of the midline. The theory that dermatofibrosarcomas originate from the mammary ridge explains the multiple skin tumors without metastases observed by Darier and Ferrand, Coenen, Willis, Usher and Bezecny. It is difficult by this theory of origin, to account for the tumors which have been observed on the wrist and on the penis. They apparently were dermatofibrosarcomas without relation to the mammary ridge, unless they could be accounted for on the basis of aberrant embryonic tissue in these situations.

Mosto,[5] studying preparations made in a case of dermatofibrosarcoma observed by Seminario and Pessano,[43] expressed disagreement with the opinion of Darier and Ferrand, who attributed a mesenchymal and therefore connective tissue origin to this neoplasm,

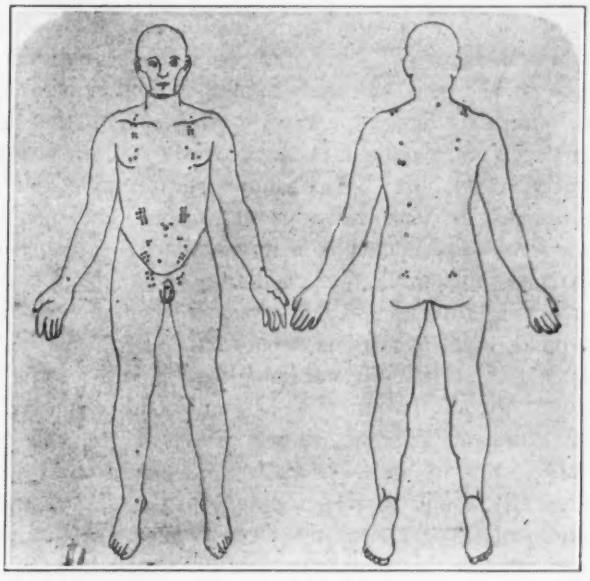

Fig. 2.—Spot map showing the situation of dermatofibrosarcoma protuberans in reported cases. The distribution suggests a relation to the mammary ridge (Binkley).

which participates at the same time of the nature of fibroma and of a sarcoma. He expressed the opinion that histologically progressive and recurrent dermatofibroma is not identical with fusocellular or fibroblastic sarcoma, for its histopathologic picture does not show the structural elements peculiar to the latter. According to Mosto,[5] the arrangement of the fine strands oriented in multiple directions which are shown in different sections made in the most varied positions makes one at first sight think of a plexiform neuroma. As a matter of fact, this plexiform arrangement is rare in purely connective tissue tumors, which show a coarser network with a larger amount of collagen and disappearance of nuclei forming subsequently thick connective tissue

strands which rapidly become hyalinized. This form of network formed by fine strands whose branches are in intimate relation with one another, constituting, as it were, beams interspersed with small filaments, evidently corresponds to the peripheral neuromas. On the other hand, there can also be adduced in favor of this opinion the characteristic palisade arrangement of numerous fibrillae and also the alinement at certain spots of chains of cells. The definite separation of the obviously collagenous connective tissue from the nervelike-appearing fibrillae presents a vivid contrast in certain areas. This can be affirmed categorically after differential staining, for Van Gieson's stain produces not a reddish but a frankly yellowish color. Mallory's phosphotungstic acid hematoxylin produces a light blue color in certain areas and a darker blue in others. With the aid of Del Rio Ortega's ammoniated carbonate of silver, splendid impregnations of nerve substrate can be obtained. In such a case neither neurites nor myelin sheaths are observed; hence the type corresponds to that of aneuritic neuroma or peripheral glioma. These tumors, by autonomous proliferation of neuroglia cells or of Schwann's sheath, give rise later, like connective tissue cells, to collagenous substance. That is to say, these tumors consist of pure neuroglia and secondarily of well vascularized connective tissue and numerous capillaries, some of them embedded in collagen. Therefore one should consider them not as fibromas or dermatofibromas but as dermatoneuromas or rather as dermato-schwannomas or peripheral dermatogliomas with some structural resemblance to the dermal tumors of von Recklinghausen. Darier,[64] however, did not contest the clinical diagnosis or the microscopic structure in Seminario and Pessano's [48] case which Mosto [5] studied histopathologically, for it fits in perfectly with the clinical and histologic characteristics of progressive and recurrent dermatofibroma. As regards the origin of this neoplasm, Darier [64] took up a point of view opposed to that of Mosto,[5] alleging that the arguments in favor of the neuritic or gliomatous theory of origin of these tumors are not convincing. Mosto's [5] theory also has been contested by Pautrier and Woringer [62] and by Scolari.[32] Mosto [5] indeed drew hasty conclusions, especially since this is a matter which requires deep study and long reflection before any definite opinion can be formed. It must be added that recently Bogliolo,[65] corroborating the opinion of Penfield,[66] Bailey and Hermann,[66] Parker,[66] Adison and Kermohan[66] and Ewing,[66] said

64. Darier, J.: Les fibrosarcomes de la peau sont-ils des dermatoneuromes? Ann. de dermat. et syph. **10**:852-855, 1929.

65. Bogliolo, L.: Os assim chamados neurinomas (ângio-fibro-blastomas; fibro-blastomas), com especial referência aos do ângulo ponto-cerebelar, Resenha clin.-cient. **12**:227-234, 1943.

66. Cited by Bogliolo.[65]

the neurinomas are blastomas of a connective tissue nature and consequently of mesenchymal origin. This theory is opposed to that of Mosto,[5] who attributes to such tumors an ectodermic origin. Alkiewicz,[54] basing his opinion on the work of Civatte [67] on the relations between histiocytoma and lozenge-shaped fibroma and guided also by his observation of a case in which there existed side by side lesions of the Darier and Ferrand dermatofibroma type of histiocytoma, concluded that the "histiocyte is a temporary evolutionary form which later becomes a fibroblast. So histiocytoma can finally evolve into a fibroma. Contrary to the opinion generally held so far, there may originate from it not only a lozenge-shaped fibroma but also a Darier-Ferrand dermatofibroma, and so the latter may at times be a histiocytoma which has undergone cure." Alkiewicz [54] admitted that in the same way that the lozenge-shaped fibroma springs from a histiocytoma the latter can also give rise to progressive recurrent dermatofibroma, as happened in his case, in which there was also evident evolution of the dermatofibroma into sarcoma. After an examination of the preparations, Civatte [67] concurred in this opinion. Favre and Josserand,[1] however, expressed the belief that the ideas about connective tissue tumors and the formations which one calls sarcomas are oversimplified and rudimentary; they stated that dermatologists ought therefore to limit themselves, for the time being, to affirming the existence of cutaneous connective tissue neoplasms which show an evident contrast between histologic malignancy and a clinically benign character as is the case with certain cutaneous neoplasms of epithelial origin. The attempts made to explain the intimate mechanism of the formation of progressive and recurrent dermatofibromas represent so far only a simple effort on the part of research workers to elucidate the unknown factors of this neoplasm as occurs with blastomas in general.

ETIOLOGY

The cause of progressive and recurrent dermatofibromas is unknown. In the great majority of cases these tumors appear without the slightest apparent cause. It is true that some authors have mentioned as a starting point an old surgical scar, nevus and even, in 1 case, a scar of lupus. But these theories give no help in unraveling the unknown cause of the curious tumors being studied. It may, however, be asked whether the scar or even the nevus constituted a weak spot of lessened resistance or functioned as an irritant and thus facilitated the occurrence of the dermatofibroma. Several authors have also reported the appearance of these cutaneous fibrosarcomas in areas exposed to previous traumatism, but they said that this factor played no part in the

67. Civatte, cited by Alkiewicz.[54]

occurrence of the tumor. In my case the traumatism of the forehead and crown of the head continued for a long time with relatively great intensity because the patient was in the habit of carrying various objects on the head, as is the habit among the rural populace in Brazil. I believe that in those cases at least in which previous traumatism exists the traumatic element can be invoked to explain the start of the disease, not as an effective cause but as an adventitious or secondary one by setting up a zone of lowered resistance, thus favoring the appearance of the neoplasm. The part played by traumatism in the localization of syphilis in certain cases is well known as well as in the origin of certain cases of leprosy and even in the predilection of blastomas for organic sectors subjected to repeated traumatism.

PROGNOSIS

The prognosis of progressive and recurrent dermatofibroma is more unfavorable than that of simple fibroma because of the resistance of the former to treatment and its tendency to continuous progression and recurrence; there may even be metastases. But the prognosis is incomparably less serious than it is for sarcoma. Early treatment well carried out has a decisive influence on the prognosis.

PROPHYLAXIS

It has not been possible to carry out efficiently the prophylaxis of progressive and recurrent dermatofibroma.

TREATMENT

The most varied forms of treatment have already been adopted for protuberant dermatofibrosarcoma. Radium therapy has been employed as well as radiotherapy, electrocoagulation, surgical excision, coagulation and excision with previous and subsequent radiotherapy. Darier [8] stated the belief that no form of treatment can prevent the progressive development of this tumor, except ample and early surgical removal. Usher [39] said that he thought that dermatofibrosarcoma resists all forms of treatment except ample removal of the tumor mass. The conclusion I have arrived at as regards the different methods of treatment employed in the cases which I have been able to study is that wide surgical removal with subsequent radiotherapy constitutes the method to be preferred. But the excision should go beyond the limits of the neoplasm and partly attain the sound tissues. The most frequent cause of recurrence is inadequate excision. When there is a sclerodermatous plaque, it should also be excised entire with inclusion of the tissues a little beyond its border. In my case I could not employ adequate treatment, because the patient would not consent to the total surgical removal of the tumors and of the fibrous plaque.

REPORT OF A CASE

O. A. S., aged 38, a Brazilian Negro farmer, born at Dores de Guanhães, State of Minas Geraes, residing at Baraunas was an inpatient at the Radium Institute (Director, Prof. Borges da Costa) under the care of Dr. Alysson de Abreu.

Family History.—The father died at 80 of a cause unknown to the patient. The mother was alive and strong at 60. She never had abortions and had nine full time pregnancies. Four children were alive and strong, and four died in early infancy of causes unknown to the patient. His relatives were healthy. There was no case of a disease similar to his in a member of his family.

Personal History.—(*a*) Physiologic: The patient smokes and drinks and is a great coffee drinker. He is a field worker and exposed therefore to all kinds of weather. His nourishment has been deficient.

(*b*) Pathologic: He said that he had had grip, malaria, worms, gonococcic urethritis and mixed chancres.

(*c*) Previous Operations: He was operated on five years previously for tumors on the hairy scalp.

History of the Present Disease.—The patient said that about six years previously, in 1938, he noticed a thickening of the hairy scalp over the forehead and crown of the head. This thickening had the appearance of a callosity and in his opinion was due to carrying heavy objects on the head. Subsequently, after a period which he could not exactly determine, there appeared on the fibrous plaque in the center of the right frontoparietal region a small tumor which continued to grow until 1939, when he had it removed by a surgeon in the Bello Horizonte Public Hospital. One year later another nodule appeared on the scar, and several others presented themselves round the site of the original nodule; all were small, except the one in the left frontal region, which grew to the size of a tangerine (fig. 3). There were no subjective symptoms. In November 1940 the patient went to the Radium Institute in this city where he was subjected to various tests, including the Wassermann, to which the reaction was positive (4 plus). It was therefore thought that his lesions were of syphilitic origin, but the specific treatment was ineffective. In July 1941 he returned home, after refusing to have the tumors removed surgically. On April 3, 1943 he returned to the Radium Institute and stated that toward the end of 1942 one of the small nodules on the right frontoparietal region had begun to grow rapidly, attaining the size of the head of a fetus. The tumor sprouted a stalk, became eroded and fell over the right eye and right side of the face (fig. 4). The nodule on the left frontal region also increased in size, becoming bosselated. The patient complained of pain and weakness, affirming that he could not see with the right eye because the large tumor formation falling over his face obstructed his vision.

General Examination.—The facial appearance was normal and the attitude active. There was lateral inclination of the head toward the left as this prevents traction on the stalk of the largest tumor and so eases the patient. The nails and hair were normal, except for loss of hair on those parts of the scalp in which there was tumor growth. Skin: There were scars left by dental fistulas on the left lower maxillary region and by ulcerated adenitis in the right groin. The skin was brown and dry and moved freely. Over the level of the forehead and crown of the head there were twenty tumors, three of which were large, the others being about the size of a hazelnut. Two of the three large tumors were situated in the right temporoparietofrontal region and the other in the corresponding

region on the left. Of the two tumors on the right one was farther forward, spreading toward the frontal region, and the other was nearer the intersection of the temporal and parietal regions. The frontal tumor was unusually large and was pedunculated, falling over the upper two thirds of the right side of the

Fig. 3.—Progressive and recurrent dermatofibroma of Darier and Ferrand. Rare implantation on the hairy scalp (in 1940).

Fig. 4.—Progressive and recurrent dermatofibroma of Darier and Ferrand.

face and totally covering the corresponding orbital region. This large tumor was circular in outline, the size of the head of a fetus, pink and measuring 14 by 17 cm., with its outer surface eroded in part and secreting a yellowish foul-smelling liquid. There were crusts which were hard to the touch. The tumor

was painless, and its surface was irregular in part and partly smooth. There was intense vascularity. The tumor was joined to the frontal region by a stalk covered with smooth, freely movable skin, which could be taken up in folds by the fingers. As the stalk was appreciably long, the large tumor mass could be raised so as to uncover the upper two thirds of the face and the orbital region. (The eyeball was in perfect condition.) It should be pointed out that it was only by so doing that the patient could use his right eye. Palpation of the stalk showed that it consisted of a hard wide fibrous cord, which was greatly stretched by the tumor. The internal surface of this tumor was smooth and concave. The skin over the tumor itself could not be taken up in folds. The second tumor, which was smaller, the size of a tangerine, was situated behind the first, with which it was confluent at its base. It was bosselated and sessile, pink, hard to the touch and eroded on the surface. The third of the three larger tumors was 6 by 5 cm. and was situated on the left side of the frontal region, hard to the touch and with an irregular bosselated surface, eroded at certain points, sessile and pink and had another excrescence on its surface. The other tumors, which were smaller than these three, showed on a smaller scale the same clinical features and were also painless. All the tumors —that is, the ones on the crown and forehead—rested on a sclerodermiform plaque which was hard, smooth and hairless at certain points and did not move over the underlying tissues. Some tumors merely appeared at the surface of the plaque.

Visible Mucosae: The visible mucosae were normal in color. The musculature was of good tonicity and the subcutaneous cellular tissue normal. The patient had a temperature of 36.5 C. [97.7 F.], was 172 cm. tall and weighed 51 kilograms. Examination revealed that the respiratory, circulatory and digestive systems, the liver and the urogenital apparatus were normal.

Lymphohemopoietic Apparatus: The epitrochlear and inguinal lymph nodes were enlarged. The spleen was not perceptible on palpation. The locomotor apparatus and the nervous system were normal. A complementary examination gave a positive (4 plus) Wassermann reaction.

SUMMARY AND CONCLUSIONS

The clinical report of a case of progressive and recurrent dermatofibroma (of Darier and Ferrand), the second case reported in Brazil, is made. There exist various synonyms for this cutaneous affection, but the name of progressive and recurrent dermatofibroma should be adopted in honor of Darier and Ferrand. The first cases of this clinical condition were described by Taylor and Sherwell in 1890 in the United States, but it was Darier, along with Ferrand and Hoffman, who gave it a definite place in human pathology. These tumors should be classified between the fibromas and the sarcomas, oscillating toward one or the other class according to the case. The classic clinical symptoms are characteristic, but in atypical cases careful interpretation of symptoms is needed for correct classification. Progressive and recurrent dermatofibromas can occur on any part of the skin, but the hairy scalp, face and penis are rare sites. In the cases hitherto reported members of the two sexes were unequally attacked, there being a visible predominance of the disease among males. Up to 1943, 124 cases

(not including Hertzler's 22 cases) had been reported in world medical literature; hence the disease can no longer be considered extremely rare, as was formerly believed to be the case. The races attacked in the descending order are: the white, the black, the yellow and the mixed. This neoplasm is of mesenchymal and therefore of connective tissue origin. The differential diagnosis must be made between this disease and localized scleroderma, keloid, Civatte's lozenge-shaped fibroma, histiocytoma and myxoma, fungoid mycosis, desmoid of the abdominal wall, von Recklinghausen's disease, Perrin's and Kaposi's sarcomatosis and other cutaneous sarcomas. In my case and in that of Yamasaki the differential diagnosis had also to be made between it and wen of the hairy scalp and the tumors called "turban tumors" by the English. The cause is unknown. The prognosis is more serious than that of fibromas but less serious than that of cutaneous sarcomas properly so-called. On account of ignorance of the cause, prophylaxis cannot be carried out. As regards the tumor in question, histopathologic examination showed it to be a dermatofibroma. The positive diagnosis of this neoplasm is clinical rather than anatomicopathologic, for these blastomas do not present characteristic and unchanging histopathologic features; these, on the contrary, vary from case to case and according to the stage of evolution of the morbid process. The best treatment is total wide excision of the tumors and of the fibrous plaque (when this is present) followed by radiotherapy.

Clinical Notes

KERATOSIS BLENORRHAGICA

GERALD A. SPENCER, M.D., NEW YORK

Cutaneous manifestations of gonorrheal infection are not a common occurrence. Now that the era of sulfonamide and penicillin medications is being passed through, gonorrheal dermatosis will in time become a still rarer observation. The case of keratosis blenorrhagica reported in this paper is of interest because it presented three unusual features: First, the clinical appearance of the infection was not the usual type. Second, the condition occurred in a woman, in whom it is not frequently encountered. Third, there was the early response to sulfonamide medication and rapid involution of the cutaneous lesion.

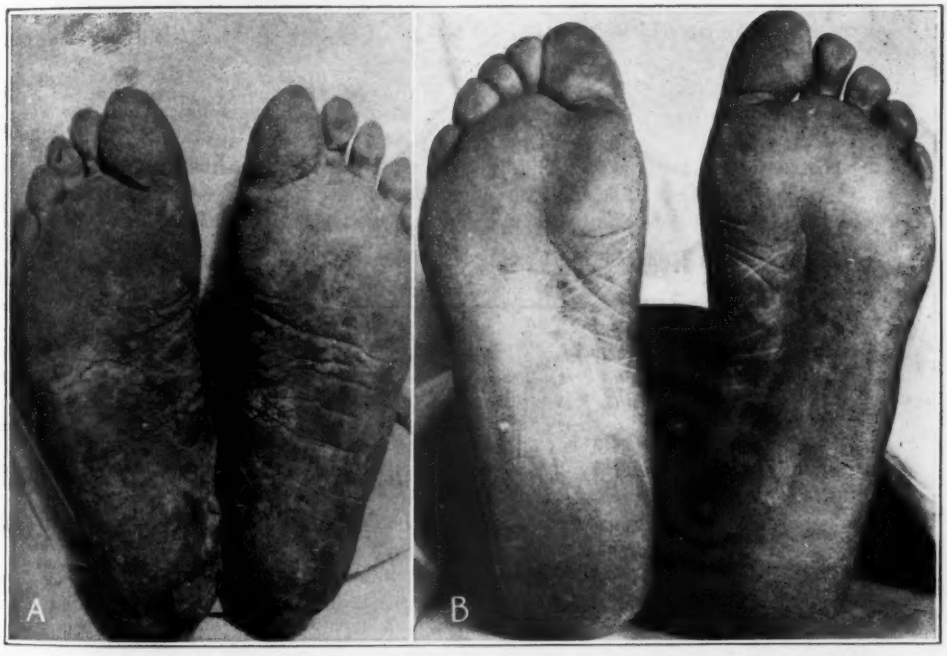

Fig. 1.—*A*, thickening and cracking of soles. *B*, complete healing of lesions on soles.

REPORT OF A CASE

H. V., a woman aged 38, complained of an eruption on the palms and soles, which extended to the legs. The onset of the disease began two months previously, when she first noticed a thickening and cracking of the soles and palms, and then a rash appeared on the legs and forearms.

Examination showed a diffuse thickening and cracking of the soles (fig. 1 *A*), which made walking difficult. On the legs there were discrete and confluent papulosquamous lesions that extended to the knees. Some of the newer papular

lesions were soft and hemorrhagic. On the palms there was a diffuse thickening, chiefly situated on the central portion, with discrete papular lesions on the borders, which thickening extended to the anterior aspect of both wrists. There were no lesions on the other portions of the cutaneous surface.

The patient denied having had syphilis or ever having received antisyphilitic medication. Further interrogation revealed that she had taken no medicaments by mouth or parenterally.

Genital examination showed that there was a profuse mucopurulent vaginal discharge. Specimens for smear and cultural examinations were obtained from the urethra and the cervix. Cultures were reported positive for gram-negative diplococci.

The Wassermann reaction of the blood was negative. No abnormalities were found in the urine. The physical examination showed no other abnormalities.

The patient then was given sulfathiazole medication, in doses of 1 Gm. tablets, to be taken every four hours for ten days. Four weeks later additional specimens for smear and cultural examinations were reported negative. At this time, the lesions on the legs had completely disappeared and the thickening of the palms and soles was considerably reduced. Two months later the palms and soles were completely free of lesions (fig. 1 *B*).

SUMMARY

A case of keratosis blenorrhagica in a woman with unusual clinical manifestations is reported.

Diagnosis was confirmed by cultural studies of material from two genital foci.

Treatment with sulfathiazole taken internally in adequate dosage brought about speedy cure of the infection, with rapid involution of the cutaneous lesions.

129 West One Hundred and Twenty-Ninth Street.

THE USE OF VIOFORM IN LOCAL DERMATOLOGIC THERAPY

THOMAS S. SAUNDERS, M.D., PORTLAND, ORE.

In a footnote in their book entitled "Dermatologic Therapy in General Practice," Sulzberger and Wolf[1] have stated that "this local remedy [Vioform, 1 to 3 per cent in petrolatum] is unfortunately not sufficiently appreciated." On the basis of extensive clinical trial, it proved to be "one of the best antieczematous, mildly soothing and antiparasitic remedies."

Not wishing to deprive my patients of such an apparently valuable remedy, I prescribed it to several suffering from superficial inflammatory diseases of the skin (eczema, tinea, eczematized dermatophytosis, eczematoid dermatitis and others). To minimize the possibility of irritation, 1 per cent of the drug in petrolatum was used. In 14 cases, the results were definitely known. The patients in 5 of these were cured either by the ointment or some measure used simultaneously, such as the avoidance of suspected contact allergens. In 5 others the disease was unaffected by the salve, and in 4 other cases the eruption became worse, apparently aggravated by the ointment.

Because the incidence of irritation was too high and the proportion of beneficial results was too low, further study of the medication was not attempted.

1020 South West Taylor Street.

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1. Sulzberger, M. D., and Wolf, J.: Dermatologic Therapy in General Practice, ed. 2, Chicago, The Year Book Publishers, Inc., 1942, p. 106.

Obituaries

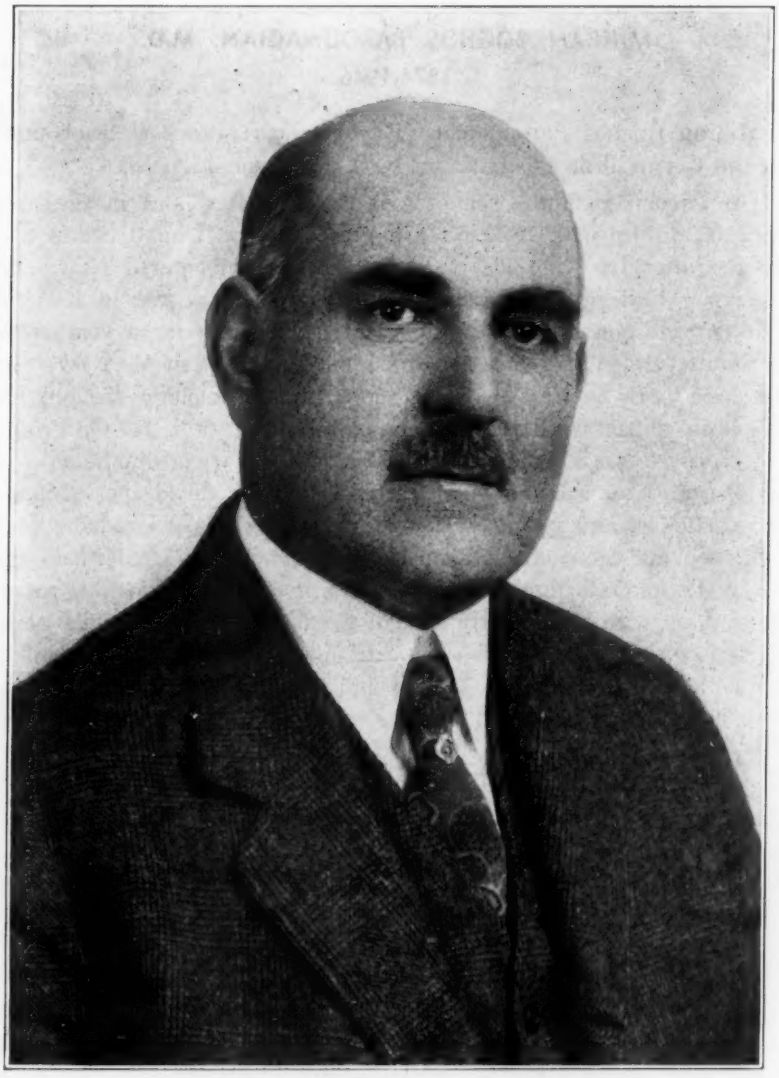
MIHRAN BOGHOS PAROUNAGIAN, M.D.
1874-1946

Mihran Boghos Parounagian died of a heart attack at his country place in Cornwall on the Hudson, N. Y., on June 13, 1946.

Dr. Parounagian, the son of a blacksmith, was born in Caesarea, Armenia, on July 10, 1874. He migrated to the United States as a boy and after receiving his preliminary education entered New York University College of Medicine; he received his degree in medicine in 1895. He entered active practice after interning for a year at the Almshouse and Workhouse Hospital on Welfare Island, New York city. His early interest in dermatology and syphilology brought him into close contact with the masters of his generation, H. G. Piffard, J. A. Fordyce and S. Pollitzer, whose tutelage and friendship he enjoyed. Dr. Parounagian was appointed instructor and then adjunct professor of dermatology and syphilology at the New York Post-Graduate Medical School and Hospital (1906 to 1916). He was visiting dermatologist to City Hospital, beginning in 1906. He never relinquished his several associations with the departments of dermatology and syphilis of the hospital system of New York. He held positions as chief of dermatology and syphilology at Gouverneur Hospital from 1910 to 1919, continuing from that time as consultant, and as visiting dermatologist and syphilologist at Bellevue Hospital and chief of the outpatient department of that institution from 1918 to 1936, after which he maintained his affiliation as a consultant. Dr. Parounagian was acting professor of dermatology at the University of Vermont College of Medicine in 1918 and clinical professor of dermatology and syphilology at New York University College of Medicine, beginning in 1929. The list of consulting posts included St. Luke's Hospital, Newburgh, N. Y.; St. Francis Hospital, Poughkeepsie, N. Y.; Medical Center of Jersey City, Jersey City, N. J.; Manhattan State Hospital, New York; Cornwall Hospital, Cornwall, N. Y.; Tuxedo Memorial Hospital, Tuxedo Park, N. Y., and Bayonne Hospital and Dispensary, Bayonne, N. J.

Dr. Parounagian was a member of the American Medical Association, fellow of the New York Academy of Medicine, member of the Manhattan Dermatologic Society and president and founder of the Armenian Medical Society. He was active in these societies, holding chairmanship in the Armenian Medical Society from 1933 to 1936 and again from 1938 to the date of his death. He was chairman of the New

York Academy of Medicine, Section of Dermatology and Syphilis, from 1926 to 1927 and was president of the Manhattan Dermatologic Society for several terms, being one of the earliest members of this society.



MIHRAN BOGHOS PAROUNAGIAN
1874–1946

Dr. Parounagian enjoyed a large circle of friends. He was tenacious in holding his friends to him. Classmates were happy to be listed among his friends over half a century after graduation. He was

a friend of his patients. He courageously fought for improved clinic facilities and made his influential friends understand his passion for the need and advance of hospital and clinical aid to the ill.

Dr. Parounagian demonstrated his theories by presenting many patients before the New York Academy of Medicine, Section of Dermatology and Syphilis, and the Manhattan Dermatologic Society. He was intense in discussion, drawing on his own experiences rather than referring to the literature of the past.

Dr. Parounagian married Sophie Phoebe Freudenburg on June 7, 1895. She survives him. Having no children, the couple devoted themselves to the children of close relatives. After a coronary incident in 1936, Dr. Parounagian curbed his professional activities at office and hospital and spent more time at his country place in Cornwall on the Hudson, N. Y.

V. BOGHOSIAN, M.D.

News and Comment

American Board of Dermatology and Syphilology.—At the recent meeting of the American Board of Dermatology and Syphilology held in San Francisco, June 28 and 29, the following thirty-nine candidates were granted certificates by the Board and may now be referred to as diplomates: Jacob Bleiberg, Newark, N. J.; Alexander M. Buchholz, Chicago; Paul Joseph Catinella, Rochester, Minn.; Harry A. Cumming, Minneapolis; Werner Duemling, San Diego, Calif.; Emanuel Montague Fainer, Los Angeles; Gerald Myron Frumess, Denver; Solomon Greenberg, Bayonne, N. J.; Moses Henry Holland, Weehawken, N. J.; Alfred Hollander, Springfield, Mass.; Alfred H. Illge, Portland, Ore.; Stanley James Joyce, Detroit; Ben Kanee, Vancouver, British Columbia, Canada; George Kien, New York; Raymond Kimbrough, Richmond, Ky.; Hans Krueger, New York; Emory Ladany, New York; Irving A. Lewe, Los Angeles; Earl Lafayette Loftis, Dallas, Texas; David Basil Morgan, Kansas City, Mo.; Edward Murphy, North Hollywood, Calif.; David J. Musman, Denver; Harry Nieman, Dayton, Ohio; Leo Orecklin, Detroit; Abraham Orfuss, New York; L. Stuart Planche, New Rochelle, N. Y.; Max Popper, Los Angeles; Charles O'Neal Rich, Salt Lake City; Harry Robinson Jr., Baltimore; Otto Ernest Lincoln Schmidt, San Francisco; Louis Schwartz, Bethesda, Md.; Oscar David Schwartz, Detroit; Abraham Albert Shapiro, Baltimore; Karl Steiner, Denver; Gordon Barclay Taylor, Hattiesburg, Miss.; Louis Henry Tobin, New York; Leonard Trilling, New York; Donald Hugh Williams, Vancouver, British Columbia, Canada, and Clyde Wood, Beverly Hills, Calif.

The following seven candidates were successful in the examinations and will be considered diplomates when they have completed five years in dermatology: Leo Marshall Columbus, San Francisco; Gage Helms, Long Beach, Calif.; Robert Wayne Helms, Long Beach, Calif.; Rodney F. Kendall, St. Paul; William Mulvehill, Beverly Hills, Calif.; Bernard F. Ryan, Los Angeles, and J. Walter Wilson, Los Angeles.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

PYODERMIC MYIASIS IN CHILDREN. LEON GOLDMAN, Am. J. Dis. Child. **69**:280 (May) 1945.

In the American tropics, cutaneous myiasis is fairly common in children. It is usually of the pyodermic type with the formation of pustules, furuncles and carbuncles. These pyogenic processes represent varying degrees of secondary infection about the larval forms of the bot or warble fly, Dermatobia hominis. This short article is well illustrated.

NELSON PAUL ANDERSON, Los Angeles.

SECONDARY SYPHILIS FOLLOWING PENICILLIN THERAPY OF GONORRHEA. DONALD W. ATCHESON, Am. J. Syph., Gonor. & Ven. Dis. **29**:423 (July) 1945.

The author reports the development of secondary syphilis in a patient who had received 100,000 units of penicillin for the treatment of gonorrhea twenty-five days previously. The course of events is of unusual value, as the patient was under complete control and observation, being confined to the Army air base; hence there was eliminated the possibility that syphilitic infection occurred after the penicillin was administered. The case report also demonstrates the inadequacy of treating syphilis with the same dosage of penicillin as that used for gonorrhea.

THE DIAGNOSIS OF GRANULOMA INGUINALE MADE BY EXAMINATION OF TISSUE STAINED WITH HEMATOXYLIN AND EOSIN. S. H. POLAYES and LEONARD WILLIAMS, Am. J. Syph., Gonor. & Ven. Dis. **29**:425 (July) 1945.

The authors corroborate the contention of Pund and Greenblatt that granuloma inguinale may be diagnosed by examination of biopsy material prepared by the usual routine—paraffin sections of tissue fixed in solution of formaldehyde which have been stained with hematoxylin and eosin. Two cases are cited by the authors illustrating the ease with which the "pathognomonic cell," with intracytoplasmic cysts containing the leishmania bodies, can be demonstrated in paraffin sections stained with ordinary hematoxylin and eosin.

THE RETARDATION AND SUPPRESSION OF EXPERIMENTAL EARLY SYPHILIS BY SMALL DOSES OF PENICILLIN COMPARABLE TO THOSE USED IN THE TREATMENT OF GONORRHEA. H. J. MAGNUSON and H. EAGLE, Am. J. Syph., Gonor. & Ven. Dis. **29**:587 (Nov.) 1945.

The evolution of early syphilitic infection in rabbits was materially modified when small doses of penicillin comparable to those used in the treatment of gonorrhea in man were administered during the incubation period.

Four hundred units per kilogram injected intramuscularly five times at three hour intervals to a total of 2,000 units per kilogram, a dose which was less than one thirty-secondth of the amount, similarly administered, necessary to cure an established syphilitic infection in rabbits, either aborted the infection entirely or significantly prolonged the incubation period. Many of the delayed lesions were so small that comparable lesions in man might well have escaped detection, resulting in infections "asymptomatic" in effect if not in fact.

With penicillin being increasingly used as a primary therapeutic measure in gonorrhea, it is probable that the number of aborted, delayed or "asymptomatically"

acquired syphilitic infections will increase. Patients receiving treatment for gonorrhea should be kept under close serologic and clinical observation for a period of at least four months and preferably longer to guard against the latter two possibilities.

STUDIES ON LIVER FUNCTION: LIVER FUNCTION IN EARLY SYPHILIS BEFORE AND DURING MASSIVE ARSENOTHERAPY. M. M. HOFFMAN and F. KALZ, Am. J. Syph., Gonor. & Ven. Dis. **29**:596 (Nov.) 1945.

The functional status of the liver was evaluated prior to, during and after massive arsenotherapy in 22 patients with early syphilis by the following laboratory tests: the blood prothrombin concentration, the serum bilirubin level, the sulfobromophthalein sodium clearance and the rate of hippuric acid synthesis.

In only 3 patients were all these factors normal before therapy was started. During massive arsenotherapy the blood prothrombin concentration was decidedly reduced in 21 patients. In 10 patients at least one of the other observations indicated impairment of hepatic function. Function of the liver returned to normal within six months after cessation of arsenotherapy in all patients in this series.

Reduction of the prothrombin level did not occur in 10 patients who received 0.06 Gm. of oxophenarsine hydrochloride (mapharsen) twice a week for ten weeks.

TREATMENT OF GRANULOMA INGUINALE WITH ANTHIOMALINE. LAWRENCE C. GOLDBERG, Am. J. Syph., Gonor. & Ven. Dis. **29**:608 (Nov.) 1945.

Sporadic reports on the use of anthiomaline (antimony lithium thiomalate), a pentavalent antimony compound, have appeared in the literature. The author reports a case in which extragenital granuloma inguinale was successfully treated with the drug.

INGUINAL LYMPHOGRANULOMA VENEREUM IN THE MALE. H. A. TUCKER, Am. J. Syph., Gonor. & Ven. Dis. **29**:619 (Nov.) 1945.

In the seven year period ending Sept. 1, 1944 750 males were admitted to the Gorgas Hospital, Ançon, Canal Zone, with lymphogranuloma venereum. The incidence was about 6 per thousand male patients admitted to the hospital. Thirty-six and one tenth per cent were white persons from the United States. No significant racial reactions to the disease or its treatment were found. Primary penile lesions were noted in 13.3 per cent of the patients; 26.9 per cent of the patients had concomitant acute venereal disease. When the patients were seen early in the course of the disease, the best results followed sulfonamide therapy alone. Sulfathiazole came to be the drug of choice. Partial adenectomy was a definite adjunct of the treatment and was unhesitatingly used if the lymph nodes were fluctuant.

REUTER, Milwaukee.

LEISHMANIASIS. ARDZROONY PACKCHANIAN, J. A. M. A. **129**:544 (Oct. 20) 1945.

Cultures of material taken from the ulcers of 2 soldiers who had recently returned from the Near East yielded Leishmania tropica. The diagnosis of cutaneous leishmaniasis usually is based on the clinical appearance of the lesion and on the presence of leishmania bodies in the stained preparations made from scrapings of the ulcer. This procedure is not conclusive, because occasionally yeastlike organisms or other extraneous substances from the lesion may be confused with leishmania bodies. If the ulcer occurs singly and is not extensive, local treatment with an ointment containing 2 per cent of antimony and potassium tartrate or local injections of 2 to 3 cc. of a 1 per cent solution of berberine sulfate have therapeutic value. When the lesions are multiple, intravenous injections of step-up doses of pentavalent antimony preparations are necessary to produce curative results.

When a suitable culture medium is inoculated with material containing aflagellar forms of L. tropica and incubated at room temperature for about ten days, a

luxuriant growth of readily recognizable flagellates is obtained. The flagellates are leptomonad in form, are actively motile and colonize on the slanted portion of the blood agar tube.

CONGENITAL CATARACTS IN SISTERS WITH CONGENITAL ECTODERMAL DYSPLASIA. H. N. COLE, HORACE K. GIFFEN, J. T. SIMMONS and GEORGE M. STROUD III, J. A. M. A. **129**:723 (Nov. 10) 1945.

Two sisters, aged 10 and 22 months respectively, had congenital cataracts, extreme internal strabismus, hypoplasia of the nails, almost complete alopecia, atrophic nasal mucosae and generalized hypoplasia of the skin. Typical major congenital ectodermal dysplasia of the anhidrotic type is considered to be a sex-linked recessive character (transmitted by the apparently normal female and affecting some of the males). However, cases have been recorded in which the ectodermal dysplasia has been classified as an incomplete dominant character (abnormality transmitted by direct descent from the diseased members of a family to some of their children, who in turn transmit it, and so on). The type of heredity in these 2 patients is considered to be of the incomplete dominant form.

COMPLETE SUBSIDENCE OF SCLERODERMA WITH DIHYDROTACHYSTEROL. EUGENE T. BERNSTEIN and LEWIS A. GOLDBERGER, J. A. M. A. **130**:570 (March 2) 1946.

A woman aged 70 underwent subtotal thyroidectomy for colloid goiter, and generalized scleroderma was observed one year after the operation. On the assumption that the scleroderma was caused by parathyroid deficiency resulting from the thyroidectomy, treatment with dihydrotachysterol was instituted. Complete regression and recession of all physical symptoms occurred with the exception of the maldistribution of pigment.

HENSCHEL, Denver.

ALLERGY TO CHEMICALS IN FLOUR: A CASE OF DERMATITIS DUE TO BENZOIC ACID. K. A. BAIRD, J. Allergy **16**:195 (July) 1945.

The author reports a case of recurrent dermatitis in a young baker, involving the face, neck, shoulders, arms and chest. Benzoyl peroxide when used for bleaching flour (improved flour) yields benzoic acid as a residue. This was considered the offending allergen.

The results of patch tests were as follows: with cake, bread and pastry flours containing "improvers," positive; with nonimproved flour, negative; with 6 per cent benzoic acid in liquid petrolatum, positive ("a definite papular rash in about six hours"); with liquid petrolatum, negative; with potassium bromate, negative.

The etiologic diagnosis was further substantiated by the fact that when the patient was entirely well a brief exposure to "improved" flour promptly resulted in a recurrence of the dermatitis.

MENDELSOHN, New York.

NATURAL ANTIBODIES AGAINST YEAST-LIKE FUNGI AS MEASURED BY SLIDE-AGGLUTINATION. CHARLES H. DRAKE, J. Immunol. **50**:185 (March) 1945.

Agglutinins active in low dilutions against a variety of cellular antigens are common in blood serums. They are usually referred to as "normal" or "natural" antibodies, and several theories have been advanced to explain their presence without any known antigenic stimulation. Drake thought that some light might be thrown on their origin if serums were tested with suspensions of several different organisms; some of these would be common in the environment and others would be met only rarely by most persons. This investigation originated from the observation that the normal rabbit serum control frequently caused agglutination in a series of tests on the antigenic relations of several yeastlike fungi. These observations also afforded an opportunity of evaluating the usefulness of "slide

agglutination" with yeastlike fungi. "Tube agglutination" is not entirely satisfactory with cellular antigens in the size range of yeast cells.

Drake found that 81 per cent of the rabbit serums, reacted to at least one organism. Saccharomyces cerevisiae was most frequently agglutinated to the highest titer (42 per cent of the serums). The pattern of these findings supports the theory that a considerable number of so-called natural antibodies represent constituents of normal serum. This is indicated by the fact that the incidence of agglutinins appears to be independent of the likelihood of exposure to a given organism.

CORNBLEET, Chicago.

SO-CALLED "PUSTULAR PSORIASIS." WILBERT SACHS and FRANCISCO SCANNONE, J. Invest. Dermat. **6**:349 (Dec.) 1945.

The authors in this presentation attempt to show that so-called pustular psoriasis is not a form of psoriasis.

They compare the pathologic features of several histologic sections of so-called pustular psoriasis with those of psoriasis and point out the difference present in the epidermis and the cutis.

It is also pointed out that these diseases differ in location, history, clinical picture and therapeutic response.

They therefore suggest that so-called pustular psoriasis may belong to the group of eczematous diseases.

PENICILLIN LOZENGES IN THE TREATMENT OF VINCENT'S STOMATITIS. LUCIAN W. STRONG JR. and ERROLL W. WILLETT, U. S. Nav. M. Bull. **46**:353 (March) 1946.

The authors report that complete cures were obtained within a period of two to five days in over 400 cases in which Vincent's infection was treated with penicillin lozenges.

The lozenges which gave the best clinical results consisted of:

Penicillin sodium	750 units
Acacia	30 Gm.
Calcium stearate	5 Gm.
Sucrose	65 cc.

The method of treatment was first to spray the mouth with penicillin solution, 250 units per cubic centimeter, and then to instruct the patient to dissolve a lozenge between the cheek and the gum every hour. A lozenge should also be chewed by the patient on retiring and at any time during the night that he awakens. Brushing of the teeth or the gums is contraindicated.

The lozenges retain their potency for four weeks when stored at room temperature.

PENICILLIN IN TREATMENT OF MADURA FOOT. HOWARD E. TWINING, HAROLD M. DIXON and FRED D. WEIDMAN, U. S. Nav. M. Bull. **46**:417 (March) 1946.

Two cases are reported in which Madura foot, contracted outside the tropics, was treated with penicillin.

In the first case, the disease, contracted in Philadelphia, was produced by the species Monosporium apiospermum in a 57 year old Italian-born man and had progressed to the development of osteomyelitis. He received 3,700,000 units of penicillin over a period of twenty-seven days, with an apparent cure at first. However, the disease relapsed, necessitating an amputation.

In the second case, the disease, contracted in Alaska, was caused by the species Cephalosporium granulomatis in a 40 year old Filipino sailor and involved only the soft tissues. He received 2,300,000 units of penicillin, and at the end of eight months the cure appeared permanent.

Since Madura foot can be caused by a number of genera and species of fungi, a precise mycologic determination should be made before penicillin treatment is instituted in order that this therapy may be properly evaluated.

RODIN, South Bend, Ind.

THE TREATMENT OF SYCOSIS BARBAE BY PENICILLIN CREAM. A. BURROWS, B. RUSSELL and H. B. MAY, Brit. J. Dermat. **57**:97 (May-June) 1945.

The authors investigated 21 cases of sycosis barbae bacteriologically and found that in 19 the eruption was caused by a strain of Staphylococcus, sensitive to penicillin. There were 13 cases in which the disease was of more than one year's duration; in 6 of these the eruption was cleared in an average time of six weeks, and in 6 there was improvement over an average period of six weeks. There were 6 cases in which the disease was of less than one year's duration; in 4 of these the eruption was cleared in an average time of two and a half weeks, and in 1 there was improvement over a period of five weeks. No improvement resulted from treatment in 2 cases, owing to the fact that the strains of bacteria were insensitive to penicillin.

The cream was prepared as follows: To 50 Gm. of Lanette wax SX (an approximately 10 per cent sulfated or phosphated mixture of cetyl and stearyl alcohol) was added 250 cc. of distilled water, and the whole was autoclaved under a pressure of 15 pounds (6.8 Kg.) for twenty minutes. Fifty cubic centimeters of castor oil was sterilized by dry heat at 150 C. for one hour. After sterilization of the oil, the two preparations were mixed and cooled to 60° C., and an appropriate amount of penicillin dissolved in water was added to make the final concentration 200 units per gram.

The patient was instructed carefully in a technic by which the cream could be aseptically removed from the jar. A knife or a spoon was sterilized in boiling water for three minutes and cooled under running tap water. The cream was then removed from the jar, spread on clean lint and applied thinly to affected areas two times a day.

THE RELATIONSHIP OF ACNE AND HYPERTRICHOSIS. E. LIPMAN COHEN, Brit. J. Dermat. **57**:102 (May-June) 1945.

The author examined 500 young women and could find no support for the statement that acne and hypertrichosis tend to occur together.

BLUEFARB, Chicago.

HAEMORRHAGIC TELANGIECTASIS. D. CAPPAN, Brit. M. J. **1**:440 (March 31) 1945.

The author reports a case of hemorrhagic telangiectasis in which there was a family history of four generations having the unusual features of polycythemia and headache following periods of anemia caused by epistaxis.

THE TOXICITY OF D. D. T. G. R. CAMERON and F. BURGESS, Brit. M. J. **1**:865 (June 23) 1945.

Experimental investigation of the toxicity of DDT (dichlorodiphenyltrichloroethane) revealed that DDT is tolerated in fairly large amounts when administered in single or repeated doses. The toxic levels are not easily reached when dilute solutions suitable for insect sprays are employed.

Human subjects whose clothing had been impregnated with DDT for prolonged periods had no ill effects.

DDT poisoning is characterized by nervous symptoms and severe damage of the liver. Usually changes in the blood picture precede the onset of the toxic stage.

CONFLUENT SMALLPOX TREATED WITH PENICILLIN. M. A. FOULIS, Brit. M. J. **1**:910 (June 30) 1945.

A patient with extremely severe smallpox was treated with a total of 800,000 units of penicillin.

The lesions failed to increase in size after penicillin therapy was started, and most of them crusted without pustulation on or about the sixth day after the eruption appeared.

Facial edema lasted no more than twenty-four hours.

SULPHONAMIDE RASHES: AN ANALYSIS OF 500 CASES SEEN IN NORTH AFRICA AND ITALY. G. A. GRANT PETERKIN, Brit. M. J. **2**:1 (July 7) 1945.

From February 1943 to December 1944 over 650 cases of cutaneous sensitivity to sulfonamide compounds were seen by the authors. These reactions were due to drugs used in the treatment of many different diseases. The largest number of cases (72.2 per cent) were of the mild sensitization type, and an additional 17.2 per cent were of the contact dermatitis type. Most cases were due to sulfanilamide in powder form.

The safest drugs appeared to be sulfadiazine and sulfaguanidine. The color and the texture of the skin were apparently of no significance in the incidence of dermatitis.

It was noted that acriflavine and cocaine can reactivate a dermatitis due to a sulfonamide compound. The author warns against indiscriminate local application of sulfonamide compounds.

TREATMENT OF EARLY SYPHILIS. C. HAMILTON WILKIE, Brit. M. J. **2**:900 (Dec. 22) 1945.

Wilkie, who is director of the venereal disease services at Leicester, England, registers a warning against the tendency to depend on penicillin alone in the treatment of acute early syphilis. He recommends penicillin plus at least one course of ten twice-weekly injections of an arsenical and a bismuth preparation.

PENICILLIN DERMATITIS. P. D. BEDFORD, Brit. M. J. **1**:51 (Jan. 12) 1946.

By means of patch tests the author proved the sensitivity of a patient to penicilin applied locally, which may have been induced by his having previously taken penicillin by mouth. He points out the risk of the haphazard use of penicillin-containing face powders and toilet applications envisaged in the popular press.

SHAW, Chattanooga, Tenn.

Society Transactions

DETROIT DERMATOLOGICAL SOCIETY

Frank R. Menagh, M.D., *President*

Hermann Pinkus, M.D., *Recorder*

Jan. 30, 1946

Discoid and Disseminated Lupus Erythematosus. Presented by Dr. Loren Shaffer and Staff of the Department of Dermatology, City of Detroit Receiving Hospital.

L. S., a Negro woman aged 27, presents typical lesions of discoid lupus erythematosus in a butterfly distribution on the nose, cheeks, eyebrows, and pinnae of both ears. She also has diffuse alopecia and dermatitis with considerable pigmentation of the scalp, posterior surface of the neck and upper part of the trunk. There is some punctate atrophy and follicular plugging on the scalp. In addition there are grouped follicular papules with a tendency to depigmentation on the back. The eruption began with a few small papules on the cheeks in June 1943. These gradually spread to the present involvement. The patient first became ill during the summer of 1944. She reported to the clinic at the City of Detroit Receiving Hospital in August 1944 with severe prostration, low grade fever and disseminated lesions at the sites of the present pigmentation. She was then sent to Eloise Hospital and Infirmary, where she remained until January 1945. Since then she has been hospitalized in the City of Detroit Receiving Hospital. She received antisyphilitic treatment from 1939 to 1942.

The Kahn and Kline reactions were positive. The red blood cell count was 3,050,000 and the white blood cell count 5,150, with 70 per cent neutrophils (45 per cent filamentous and 25 per cent nonfilamentous cells). Biopsy specimens were taken from the face in August 1944 and from the back in January 1945. Both showed changes typical of lupus erythematosus. The patient evidently received injections of oxophenarsine hydrochloride and a bismuth preparation at Eloise Hospital and Infirmary.

DISCUSSION

Dr. Franz L. Blumenthal: I have seen this patient for some time at Eloise Hospital and Infirmary. Clinically, she showed all the characteristics of lupus erythematosus discoides of the face. On the body there was a grouped papular eruption looking much more like a lichenoid tuberculid than a syphilid. Since at that time, however, the Kahn reaction was strongly positive, antisyphilitic treatment was started. Today the patient's condition is much worse. The whole eruption is of much more acute character on the face as well as on the body, but the eruption on the body still looks mostly like some form of tuberculid.

Dr. A. C. Curtis, Ann Arbor, Mich.: I was interested in seeing this case. It has seemed to me that the most extensive follicular plugging that one finds in lupus erythematosus is seen in Negroes. Why is this true? I believe that this Negro woman has disseminated lupus erythematosus of the subacute type.

Dr. Frank R. Menagh: Has this woman shown any elevation of temperature?

Dr. Loren Shaffer: She had a fever all the time she was at Eloise Hospital and Infirmary; however, the temperature was only 99 to 100 F. Since she has been here, her temperature has been normal. She shows pronounced prostration, which is characteristic of the general disseminated type. I think that it is unusual to see the combination that is seen in this case. In addition to the lupus erythema-

tosus, she has some lesions on the back in which I am interested; these are grouped follicular papular lesions with a tendency to leukoderma. Scattered disseminated lesions of lupus erythematosus with hyperpigmentation are also present on the back. I feel that these grouped papular lesions are probably atypical lichen scrofulosorum.

DR. FRANZ L. BLUMENTHAL: We thought for some time that perhaps there was secondary syphilis; but, finally we came to the conclusion that we had to deal with some kind of tuberculid.

DR. FRANK R. MENAGH: Would any one like to say anything about treatment?

DR. ALBERT J. BOYLE (by invitation): I have read considerably in connection with this case and have noted the many features it has in common with cases of adrenal lesions. The patient has had persistent headache, fever, attacks of diarrhea, loss of weight, anemia, lesions of the mouth, low blood pressure, pigmentation and other symptoms and signs, all of which may be found in Addison's disease. She has menorrhagia, which might readily account for the anemia. Also she has syphilis. Occasionally syphilis is responsible for lesions of the adrenal cortex. It does seem, however, that lupus erythematosus disseminatus has many signs and symptoms compatible with disease of the adrenal cortex.

Recently it has been shown that the treatment of Addison's disease is assisted in some instances by the administration of testosterone. On this basis I should like to see this patient given testosterone. Incidentally, I believe that there has been reported a case of successful treatment of lupus erythematosus disseminatus by roentgen therapy to the ovaries, which leads one to speculate on the hormonal aspect.

DR. FRANK R. MENAGH: In how many cases have changes been shown in the adrenal cortex?

DR. ALBERT J. BOYLE (by invitation): I have never seen figures on this point. It is conceivable, however, that there are only selective functional changes of the cortex (production of ketosteroids), not structural changes of the whole cortex, and therefore there may be no demonstrable pathologic alterations.

DR. A. C. CURTIS: In view of what has just been said, I should like to mention an article by Levine (Contratto, A. W., and Levine, S. A.: Acute Lupus Erythematosus Disseminatus, *New England J. Med.* **221**:602, 1939). His patient, like many other patients who have disseminated lupus erythematosus, was a young woman. Levine expressed the belief that an abnormality of the production of ketosteroids might have something to do with the causation. So the patient was sterilized. She died of pneumonia three months after the sterilization but had no active lesions at the time of death.

I have sterilized 2 patients with acute lupus erythematosus by radium. One woman was severely ill and had been studied for five years because of an unknown fever before the typical lesions of disseminated lupus erythematosus finally developed. Her sterilization occurred five years ago, and she is well today.

In a recent article in the *Annals of Internal Medicine* by Rose and Pillsbury (Rose, E., and Pillsbury, D. M.: Lupus Erythematosus [Erythematodes] and Ovarian Function: Observations on a Possible Relationship, with Report of Six Cases, *Ann. Int. Med.* **21**:1022, 1944), the cases of 5 patients who were sterilized are reported. Their results also are suggestive of improvement in some cases. Because in so many cases acute disseminated lupus erythematosus occurs in young women, I believe that sterilization is justified in some instances.

A Case for Diagnosis (Leukemid; Contact Dermatitis?). Presented by DR. LOREN SHAFFER and Staff of the Department of Dermatology, City of Detroit Receiving Hospital.

N. C., a white woman aged 71, presents rather sharply defined acute erythematous dermatitis of the "V" of the neck and upper part of the chest. Similar lesions are present in the cubital fossae and on the intimal aspect of the left knee.

The patient has had chronic stasis dermatitis and ulceration of the left ankle for many years. In March 1944, an acute dermatitis developed on the left leg. This was considered simple stasis dermatitis, and ligation of the saphenous vein was performed in July. The dermatitis, however, did not improve but spread to the neck and arms in September. Leukemia was first diagnosed in July 1944. At that time she had 39,000 white blood cells, including 94 per cent lymphocytes. She received 600 r of filtered roentgen rays to four areas of the anterior surface of the trunk in September 1944, after which the pruritus and dermatitis disappeared completely. The white cell count of the blood dropped to 10,500 with 69 per cent lymphocytes. The white cells have been increasing gradually; the last count was 17,300 on November 27.

The present condition suggests dermatitis venenata; however, the patient feels that it is similar to that of the previous attack, which responded well to high voltage roentgen ray therapy. The case is presented as an instance of a possible toxic manifestation of leukemia. No biopsy was performed. Results of other laboratory examinations were noncontributory.

DISCUSSION

DR. JAMES R. ROGIN: I am willing to accept the diagnosis of leukemic pruritus, but I do not see how one can call it leukemid.

DR. CLYDE HASLEY: I think that these lesions are due to stasis dermatitis, inasmuch as they appeared mainly on the ankles and legs, and I am inclined to think that is an important factor. The leukemia is probably a secondary consideration; but inasmuch as the blood count was greatly reduced with radiation one certainly has to take into consideration this contributing factor. It is hard to reconcile these lesions with a diagnosis of leukemid.

DR. HERSCHEL ZACKHEIM (by invitation): Previous treatment had not relieved the itching of the legs, but after roentgen therapy the itching subsided. Later, however, the itching began to reappear, and the blood count showed a rise.

DR. FRANK R. MENAGH: It is notable that in some cases of lymphoblastoma, particularly the Hodgkin type, one does not get too good a result, so far as the pruritus is concerned, immediately following therapy with roentgen rays. This patient volunteered the information that she painted the lesions on her ankles with a balsam salve.

DR. LOREN SHAFFER: Nobody has mentioned the erythema and dermatitis around the neck of this woman. It is suggestive of a contact dermatitis. The question is: Is this a contact type of dermatitis, or is it a manifestation of leukemia? She had a similar dermatitis before, which was not relieved by any local application until she had high voltage roentgen ray therapy. Then it disappeared and subsequently reappeared with an increase in the blood count. I questioned the diagnosis of leukemid, and I agree that the typical leukemid is a papular eruption. It does not necessarily contain the infiltration of the skin; however, I suspect because of the varied distribution of the lesions on the neck that it was actually a contact dermatitis.

A Case for Diagnosis (Superficial Epitheliomatosis?). Presented by DR. JAMES R. ROGIN.

A. E., a white man aged 45, first noticed spots on the middle of his chest and in the sternal region, as well as over his spine, about fifteen years ago. These lesions have been slowly progressive in size and in number during the past fifteen years but have at no time produced any symptoms, and he would not be conscious of them at all, except for being able to see those on his chest. He has enjoyed good health, and there is nothing significant in his general medical history. Serologic tests for syphilis have elicited negative reactions previously and do so at present.

The patient presents over the midsternal region and scattered on the chest maculopapular discrete lesions, varying in size from that of a split pea to that of a half-dollar. For the most part these lesions begin discretely, but in some places they become confluent. They vary in color from a light fawn to a deep brown, almost black. They are covered with a scale, but when the patient was first seen a few weeks ago, before treatment, most of the lesions were covered with rather tightly adherent thick crusts. Similar lesions are present over the spine, from the cervical to the lumbar region.

Crusting has disappeared for the most part after the use of a mild ammoniated mercury and salicylic acid ointment. Most of the lesions show a definite smooth white atrophy, and some of the newer lesions, for example, the one on the left side of the chest from which the biopsy specimen was taken, showed atrophy with diffuse reddish telangiectasia on the surface. This telangiectasia is not perceptible in the older pigmented lesions. The most striking feature of the lesions at present is the combination of pigmentation, atrophy and telangiectasia.

Histologic sections were presented.

DISCUSSION

DR. HOWARD PARKHURST, Toledo, Ohio: This is one of the few cases of this disease that I have seen in which the patient did not have psoriasis. I do not know whether this man gives any history of having received arsenic at any time. I was interested to note that the lesions were limited strictly to the area from the waistline up and that he stated that he had gone with his trunk exposed to the sunlight for a number of summers several years ago, prior to the development of this eruption. Whether or not the light may have been a factor is of great interest, it seems to me.

DR. A. C. CURTIS, Ann Arbor, Mich.: I thought that this eruption was rather typical of intraepithelial epithelioma, possibly Bowen's disease. The pigmentation and the distribution were unusual. By tangential light a threadlike rim was seen about some of the lesions. I agree with the diagnosis of superficial epitheliomatosis.

DR. HERMANN PINKUS, Monroe, Mich. (demonstrating the microscopic section on the screen): Most of the surface of the section unfortunately is denuded of epithelium. This is probably the result of medication. Thus one cannot say to what extent and in which form epitheliomatous changes were present. Only one end of the section is covered with epidermis, and there is a small cluster of cells of basal type within or just below the epidermis. This spot permits one to make a diagnosis of superficial epithelioma of basal cell type.

DR. A. C. CURTIS, Ann Arbor, Mich.: Well, the pathologic section is not characteristic of Bowen's disease, but it is characteristic of an intraepithelial epithelioma of the basal cell type.

DR. FRANZ L. BLUMENTHAL: I could not find much moisture in the lesions, which I assume to be characteristic of Bowen's disease.

DR. JAMES R. ROGIN: Before this man had any medication, which consisted of an ointment of ammoniated mercury and salicylic acid, the lesions were crusted; hence I thought for a time the eruption might be Darier's disease. But after a week of medication, the patient came back with the crusts all gone and the lesions as one now sees them. He has had no medication now for the past ten days.

A Case for Diagnosis (Lupus Pernio; Sarcoid?). Presented by DR. LOREN SHAFFER and Staff of the Department of Dermatology, City of Detroit Receiving Hospital.

F. S., a white woman aged 48, presents a confluent infiltrated granulomatous lesion involving the cheeks and nose. A similar lesion is present on the outer aspect of the left arm and is approximately 5 cm. in diameter. The lesions are elevated and bluish red and have a smooth surface. No searing or apple-jelly nodules are demonstrated.

The disease began sixteen years ago with a bluish red nodule on the right cheek. This gradually increased to the present size and has been stationary for several years. The lesion on the left arm began several years ago. The patient has been under observation for some years at Harper Hospital. She first reported to our clinic in June 1944. She received twelve low voltage roentgen ray treatments of 70 r, unfiltered, at weekly intervals to September 20. The lesions improved decidedly with this treatment, and the patient was able to get a job. She returned on Jan. 12, 1945 with the present recurrence.

A roentgenogram of the chest on January 12 showed that the patient had had parenchymal tuberculosis. Nodular exaggeration of the root zones raised a question of Boeck's sarcoid or possibly lymphoblastoma. A microscopic section obtained from Harper Hospital revealed epithelioid cell tubercles in the deeper parts of the corium. This is characteristic of the lupus pernio variety of sarcoid.

DISCUSSION

DR. GEORGE VAN RHEE: I saw this patient at Harper Hospital. The clinical diagnosis at that time was sarcoid, and microscopic examination confirmed this.

DR. JOHN H. COBANE: The pathologic sections are typical of sarcoid and not of lupus vulgaris. There are some nodules in her lung, and I feel from the roentgenograms of her lung that the diagnosis is sarcoid.

DR. LOREN SHAFFER: I might say that I presented this case, and it was my impression, which is evidently wrong, that the patient had been under care at Harper Hospital with the diagnosis of lupus tumidus; however, the biopsy establishes, I think, beyond question the diagnosis of sarcoid. It would be interesting to get a roentgenogram of the phalanges. She had eight injections of oxophenarsine hydrochloride without improvement. Incidentally, sarcoid will occasionally respond to the arsphenamines.

Lymphoblastoma. Presented by DR. LOREN SHAFFER and Staff of the Department of Dermatology, City of Detroit Receiving Hospital.

H. W., a Negro aged 55, has an enormous tumor, measuring approximately 14 by 16 cm., which is granulomatous and elevated approximately 4 cm. and presents areas of ulceration. The tumor is firm. The cutaneous surface, where not ulcerated, is smooth and shiny and moderately fixed. The mass extends from the fifth rib to the umbilicus. There is moderate bilateral axillary adenopathy. The patient appears otherwise in good health and has relatively little discomfort.

Approximately fifteen months ago the patient noted a small subcutaneous nodule on the abdomen near the xiphoid process. This increased slowly in size for three months and then rapidly for the past year. He has had no pruritus and says that he has had no cutaneous lesion at this site. The Kahn reaction of the blood was negative on Jan. 21, 1945. The hemoglobin was 8.5 Gm. and the white blood cells 6,700, of which 90 per cent were neutrophils. Another blood count, on January 25, showed 7,500 leukocytes, with 82 per cent neutrophils (71 per cent filamentous and 11 per cent nonfilamentous), 10 per cent lymphocytes, 6 per cent monocytes and 2 per cent eosinophils. A roentgenogram of the chest was reported as showing no specific evidence of metastatic malignant growths in the chest, ribs or dorsal portion of the spine. Three histologic sections are presented: (*A*) abdominal mass; (*B*) axillary nodes, and (*C*) skin of the abdomen near the tumor.

Pathologic Report (Dr. Bert E. Stofer): Microscopic examination of the abdominal mass (*A*) shows a nonencapsulated tumor composed of fairly densely packed cells which vary considerably in size and shape. The majority exhibit a fairly dense nucleus and scant eosinophilic cytoplasm which tends to become fibrillar in some areas. Mitotic figures are seen. Microscopic examination of the axillary tissue (*B*) shows hyalinized tissue infiltrated with cells identical to those found in the tumor mass. No nodal tissue is recognized. Tumor cells are seen invading the nerve sheaths. Microscopic examination of the skin (*C*) shows a ribbon of cells in the upper part of the corium, extending in some areas into the

papillae and into the subcutaneous tissue and the panniculus adiposus. It is in this section that the tumor cells show their greatest variability. Mitoses are frequent, and giant cells with up to four nuclei are relatively common. The chromatin in some areas is rather dense and in other areas decidedly granular. The accessory organs of the skin are surrounded by masses of tumor cells. The final diagnosis was lymphoblastoma. The exact type cannot be determined from these slides alone. The tumor itself suggests reticulum cell sarcoma. The cutaneous sections are more suggestive of mycosis fungoides or leukemia cutis. Imprint preparations, studies of bone marrow and repeated blood counts are suggested.

DISCUSSION

DR. R. C. JAMIESON: I have nothing to say. I do not think that this case belongs to a dermatologist.

DR. LOREN SHAFFER: An unusual feature of this case is the general condition of the patient. His physical condition is surprisingly good. Roentgenograms of the chest revealed no abnormalities. I made the suggestion on the record that the tumor would probably be radiosensitive. It began as a nodule and has rapidly mushroomed, especially during the past year. The pathologic picture would suggest mycosis fungoides.

DR. A. C. CURTIS, Ann Arbor, Mich.: Some time ago we saw an infant who had vulvar lesions suggestive of the changes seen in these sections. We have followed her for five months. The lesions cleared rapidly with roentgenotherapy. The last roentgenogram showed a punched-out area in the pelvis due to metastasis. This patient has a cellular response of the reticulum type, and the tumor is a lymphoblastoma.

Blastomycosis. Presented by DR. LOREN SHAFFER and Staff of Department of Dermatology, City of Detroit Receiving Hospital.

T. C., a Negro aged 45, presents a sharply defined granulomatous lesion with elevated slightly verrucous borders which involves the axillary surface of the left arm, extending from the axilla to the middle of the arm. Partial healing has occurred in the central areas. The borders of the lesion have arciform configuration, and some superficial ulceration is present in the borders.

The lesion began two years ago as a small papule which slowly increased in size. The patient consulted various physicians and received local therapy and at one time six injections of an arsenical. Repeated serologic tests have elicited negative reactions. He reported to Dr. Franz Blumenthal in August 1944 and received roentgenotherapy and potassium iodide by mouth. He improved with this treatment but discontinued it, and the disease relapsed. Roentgenograms revealed no extension of blastomycosis in the chest and left shoulder girdle. Kahn and Kline reactions of the blood were negative; other examinations were not significant.

Histologic sections show chronic granulomatous inflammation with abscesses and atypical proliferation of the epidermis. Numerous blastomycetes are present in giant cells and free in the tissue. Sulfonamide compounds have been used locally and internally for the last several weeks. Improvement is questionable.

DISCUSSION

DR. FRANZ L. BLUMENTHAL: I saw the patient last summer and found organisms in the pus. Orally he got 1 Gm. of potassium iodide three times a day and twice weekly intravenously 10 cc. of a 10 per cent solution of sodium iodide, combined with 100 r of roentgen rays filtered through 2 mm. of aluminum weekly for five weeks. With this treatment he improved greatly, but then he left the city. Today he is in much better shape than he was when I saw him the last time. At the time I saw him first he showed all the clinical characteristics of blastomycosis.

Lichen Ruber Moniliformis Kaposi. Presented by DR. HERMANN PINKUS for DR. FELIX PINKUS, Monroe, Mich.

M. M., a white woman aged 19, was previously presented at Grace Hospital in October 1937, at Harper Hospital (American Academy of Dermatology and Syphilology) in January 1938 (ARCH. DERMAT. & SYPH. **38**:317 [Aug.] 1938) and at Henry Ford Hospital in January 1942. Previous suggested diagnoses were: pyogenic infection with keloid formation, due to trauma; psoriasis; lichen planus; pyodermatitis; artefacts; keloid and larva migrans. The patient supposedly had smallpox at the age of 8 months and infantile paralysis at the age of 21 months. She wore a brace for several months which caused irritation and recurrent blisters on the legs and ankles up to the age of 4 years (a younger brother has epidermolysis bullosa). She had scarlet fever in January 1935. This was followed by a generalized vesicular (?) eruption which was treated with ammoniated mercury. The patient was in University Hospital, Ann Arbor, Mich., in May 1936, at which time a biopsy was made. The lesions cleared, except those on the legs, which have persisted ever since. Various forms of treatment, including occlusive dressings, brought temporary improvement. Additional biopsies were performed at Grace Hospital (1937) and at Henry Ford Hospital (1942).

Examination on Oct. 21, 1944 showed the patient to be well developed and well nourished. Cutaneous lesions were confined to the legs and, to a minor degree, the thighs. The legs showed a bizarre picture of bluish red firm elevated cords forming an irregular network on the anterior and lateral sides of the legs and dorsa of the feet. Some lesions were present on the calves and on the thighs. The cords were up to 1 cm. wide and almost as high, and their surface was partly shiny, partly covered with a thin silvery scale and partly crusty. They exhibited deep transverse furrows at irregular intervals, and numerous white milium-like bodies were visible below the surface. Within the meshes of the network and in the surroundings there were numerous brownish red flat or slightly umbilicated papules. The patient said that the lesions itched and hurt, and she admitted that she scratched a good deal and had the habit of digging the milia out with a needle.

Five superficial roentgen ray treatments of 72 r were given at weekly intervals to each of five fields on the anterior and lateral surfaces of the legs. The thighs were shielded from the rays. Arsenic in increasing doses was taken by mouth from October 1944 to Jan. 6, 1945. No topical treatment was advised. The patient was admonished not to scratch or otherwise injure the skin. After four roentgen ray treatments (Nov. 18, 1944) the lesions were much flatter and began to get more silvery scales. The milia had almost disappeared. Subjective symptoms were much improved. On Jan. 6, 1945 there was some edema of the legs, and the lesions were more painful and succulent, with several vesicles and bullae up to the size of a pea on the crests of the cords. This reaction was considered as due to arsenic, and vitamin B complex capsules were substituted. At present, the lesions show continuing improvement and are much flatter throughout, and some have disappeared leaving atrophic scars. Milia have become more numerous again.

Histologic Examination: Section of a "keloid" band from the right shin (Oct. 12, 1944) was reported on as follows: The epidermis is atrophic and hyperkeratotic. Several cystic dilated sweat ducts filled with horny matter and resembling milia are found in the upper part of the corium. The corium has the structure of a vascularized scar in which the elastic fibers are absent. There are scattered lymphocytic infiltration and some small clusters of mast cells. Section of a small flat papule from the left thigh (Nov. 11, 1944) revealed that there are acanthosis and hyperkeratosis, with increased mitotic activity and formation of epithelial giant cells in the epidermis at the periphery of the lesion. The central part shows separation at the dermoepidermal junction and hyalinization of the basal membrane or of the entire papillary body, with the epidermis undercutting the hyalinized portion. There is slight subepidermal cellular infiltration around numerous capillaries. Many melanophores are present.

DISCUSSION

DR. HARTHER L. KEIM: This is the fourth clinic at which this girl has been presented. She was seen at Henry Ford Hospital on one occasion, and she was shown at Grace Hospital, too. I was interested in the histologic sections. Of course, I have not the time to go into a discussion of whether or not lichen ruber moniliformis is a variety of lichen planus, but I shall refer briefly to the work of Wise and Rein (ARCH. DERMAT. & SYPH. **34**:830 [Nov.] 1936). They were convinced that it was an entirely different thing and based their opinion largely on the histologic picture. In their article they showed these areas of necrosis of the epithelium, which they stated are rather characteristic, and pointed out the absence of any characteristic lichen planus infiltrates below the epithelium. In the section which was taken in 1942 it is interesting to note that there is shown one of these typical necrotic lesions, but to my mind the cellular infiltrate in the corium is compatible with the diagnosis of lichen planus. So perhaps this is a good example of a transitional case. In 1938 the consensus was lichen planus.

DR. ARTHUR E. SCHILLER: At the time the patient was seen at Grace Hospital, the picture was different. The raised portions were verrucous and covered with much more scale. I think that the diagnosis then was lichen planus.

DR. FELIX PINKUS (by invitation), Monroe, Mich.: In my opinion the cutaneous eruption of this woman is the same disease one finds in the atlas of Kaposi (also *Vierteljahresschrift für Dermatologie und Syphilis* **18**:571, 1886) called by him lichen ruber moniliformis. There is a bundle of red brown stripes, equally elevated and equally wide, radiating down the anterior surface of the legs from a narrow center on both knees. Some of the stripes end free at the sides of the calves and on the backs of the feet and on the ankles. Most of them cross one another at acute angles, forming lozenges. Much of the free space of these rhombi is filled with one or more small papules of the same color as the stripes. These papules are similar to lichen planus. There are many clinical and histologic features which are similar to those of the case of Kaposi, although there are some important differences in all the biopsies my son has made. On the other hand, the structure in this case does not resemble the histologic picture of the best American case, that of Dr. Wise and Dr. Rein (ARCH. DERMAT. & SYPH. **34**:830 [Nov.] 1936). There is another point which distinguishes this case from a case of real lichen planus, that is its beginning. Many years ago, the disease started as a bullous eruption diagnosed as epidermolysis bullosa, and now there is the most interesting fact that in the younger brother of this patient, at the same age as it happened to his sister, blisters developed following trauma that cannot be diagnosed otherwise than as epidermolysis bullosa. So far we were inclined to accept the suggestion of Wise and Rein to separate lichen moniliformis from the typical lichen planus, to leave the diagnosis undecided and to substitute the desigation of Wise and Rein, "morbus moniliformis." Today we got some slides of an older biopsy specimen, made by Dr. Menagh, and in them the picture is rather different. There is heavy infiltration and certain changes in the epidermis, similar to the description of Kaposi. So we have to start once more, returning to the old case of Kaposi by which the question began in 1886.

DR. FRANK R. MENAGH: I think that this might be the case that connects the two groups.

DR. A. C. CURTIS, Ann Arbor, Mich.: The patient was seen by Dr. Davis in Ann Arbor in 1935, and the eruption was alleged to have appeared after scarlet fever eighteen months before. That would date the beginning as 1933. When the patient was seen in 1936, the question was whether the eruption was an atypical lichen planus or a pyoderma. Dr. C. W. Weller did not think that the infiltrate was characteristic of lichen planus. I have wondered since seeing the patient whether this was not a keloidal response in a person who has had an infectious process in lesions of lichen planus.

DR. FRANK R. MENAGH: I think that all agree that this case takes a great deal of "steam" out of Wise and Rein's paper.

DR. HERMANN PINKUS, Monroe, Mich. (demonstrating microscopic slides on the screen): Through the courtesy of Dr. Curtis, we have the section taken at Ann Arbor, Mich., in 1936. The main feature of this specimen is the cysts lined with cornifying stratified squamous epithelium and apparently formed by the sweat ducts just beneath the epidermis. The corium is fairly vascular, but there is hardly any cellular infiltration. The epidermis is thin and partly torn off. The histologic picture is similar to that of the most recent biopsies.

The specimen removed at Henry Ford Hospital, a section of which Dr. Menagh lent me, shows a different picture. In it one sees similar cornified cysts in the upper part of the corium, but, in addition, one sees a dense cellular infiltration consisting of lymphocytes and leukocytes in a vascular stroma. The epidermis is partly necrotic and partly covered with a thick scaly crust. Close to the edge of the lesion there is much atypical proliferation of the epidermis. It is quite possible that a great deal of this inflammatory reaction is unspecific and due to trauma and secondary infection. I doubt that the epidermal necrosis of this section may be compared with the peculiar necroses described by Wise and Rein. These authors performed ten biopsies on their patient and were surprised at the small amount of inflammatory infiltration they found. My father and I were similarly surprised when we performed biopsies in our case, and the first one at Ann Arbor, Mich., also shows this lack of cellular infiltration. It has been suggested that this lesion represents a keloidal change following either lichen planus or trauma. I think that the great vascularity speaks somewhat against keloid, and it must be remembered that the second biopsy specimen taken by me is from a small early papule.

Epidermolysis Bullosa with Formation of Scars and Milia. Presented by DR. HERMANN PINKUS.

D. M., a boy of 9 years, is the brother of M. M., the woman with lichen ruber moniliformis. He also was presented to this society at Henry Ford Hospital. For several years blisters have been developing over pressure points, particularly on the feet, knees and elbows. Some of these blisters leave scars in which white kernels accumulate. The patient presents a tense thick-walled bulla just proximal to the nail of the right third toe. There are several atrophic scars on the shins, knees and elbows. At the knee and elbows there are also red slightly raised firm plaques, the largest 2 by 1 cm., in which are embedded firm whitish bodies of pinhead size which resemble milia.

DISCUSSION

DR. LOREN SHAFFER: I think that this case is extremely interesting, and the papular infiltrated lesions are suggestive of the same process (lichen ruber moniliformis) as noted on the woman presented. Unfortunately, there has been no biopsy. Another interesting thing to me would be the suggestion that this disease may be familial. As far as I am concerned, I think that probably the child has two different diseases, the epidermolysis bullosa, which is not active, and these new lesions, which are papular infiltrations.

NEW YORK ACADEMY OF MEDICINE, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Harry C. Saunders, M.D., *Chairman*

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Feb. 6, 1945

Circinate Sarcoid (Boeck's). Presented by DR. ABRAHAM WALZER.

A. H., a clerk selling fruit, is presented from the dermatologic clinic of the Jewish Hospital of Brooklyn. There is no history of tuberculosis or diabetes in

the patient or in his family. He had a penile chancre for which he was treated by intramuscular and intravenous injections. The Wassermann reaction of his blood was strongly positive. After being treated for a number of months he was told that the Wassermann reaction had become negative, and treatment was discontinued. About six years later, or seventeen years ago, he married, and at that time the Wassermann reaction of his blood was said to be negative. His wife subsequently gave birth to three children, their ages at present being 15, 14 and 11 years. The Wassermann reactions of their blood, as well as that of his wife's blood, have always been negative.

About two years ago he noted "red spots" on his legs, which gradually increased in size and extent. The lesions on the face appeared about six months later. They did not itch. About six months after the onset of the rash he was seen by his physician who, in the course of a general examination, found that the Wassermann reaction of his blood was strongly positive. He has since been treated for syphilis at a local clinic.

At present the patient shows the following lesions: 1. There are large rings on the right leg and thigh, varying from 1 to 5 or 6 inches (2 to 12 or 15 cm.) in diameter. The border is about ¼ inch (0.6 cm.) in width, raised, hard, nodular, of a violaceous color and sharply demarcated. The skin within the ring is faintly pink and soft and gives a suggestion of atrophy. In one of the larger-ringed lesions of the leg, the central part is brown and feels somewhat indurated. 2. The left leg and thigh also show similar annular lesions which have joined and formed large serpiginous patches with similar raised red indurated borders, enclosing a brown indurated area within which are coin-sized patches of apparently normal skin. 3. The cheeks, the forehead and the temporal areas show flat raised erythematous plaques the size of a dollar or larger. They are smooth, indurated and not sharply outlined. Some show superficial telangiectatic vessels.

A complete physical examination, including neurologic and ophthalmologic ones, revealed nothing abnormal. Roentgenograms of the chest showed perihilar adenopathy. Roentgenograms of the hand showed a normal structure. The results of the hematologic studies, including those for total lipids, cholesterol and phospholipids, as well as blood sugar, were within normal limits. A urinalysis showed nothing abnormal. The Wassermann reaction of the blood was positive, but the Wassermann reaction of the spinal fluid was negative. An intracutaneous test with tuberculin in a dilution of 1:10,000 elicited a negative reaction.

A histologic examination of two sections, one removed from the face and the other from the leg, showed the following changes:

Lesion of the Face: Throughout the upper part of the cutis there were numerous epithelioid cells arranged in small masses (tubercles), with little or no surrounding cellular reaction. There was considerable interstitial edema in the subepidermal region, with scattered giant cells. The overlying epidermis showed no important change.

Lesion of the Leg: Throughout the entire cutis there were numerous tubercles composed of epithelioid cells and giant cells, with no central necrosis. In the upper part of the cutis the vessels were dilated and the walls thickened. There was a mild diffuse small round cell and wandering connective tissue cell exudate. The overlying epidermis was irregularly acanthotic.

DISCUSSION

Dr. Eugene Traugott Bernstein: This is a classic case of the annular type of sarcoid. The histologic picture showing naked epithelioid tubercles pathognomonic of this entity confirms the clinical diagnosis.

Dr. Louis Chargin: Obviously the eruption is not syphilis. Whether one is dealing with sarcoid or necrobiosis, it is not easy to tell. The eruption closely resembles that of a patient presented by Dr. Silver last month; in diagnosing it most discussers agreed on necrobiosis. The histologic picture of sarcoid is not at all rare in necrobiosis. Perhaps a point against this diagnosis is the sex of the

patient, the lipid disturbances being more frequently observed in women. Moreover, the lesion on the face would fit in better with sarcoid.

DR. ABRAHAM WALZER: When a lesion is shown by histologic examination to be definitely sarcoid, it must be accepted as such. However, when the histologic designation is "sarcoid-like," it does not necessarily imply sarcoid. There are sarcoid-like structures associated with tuberculosis, leprosy and other diseases, as well as with some reactions to injected foreign bodies. These lesions are no more true sarcoid than a lichenoid structure is true lichen planus. In the patient presented the lesions on the face are unquestionably sarcoid, both clinically and histologically, while those on the legs may be questioned clinically. With a definite histologic report of sarcoid, those lesions too can be nothing but sarcoid.

DR. LOUIS CHARGIN: The histologic slides in the case presented last month were declared by Dr. Sachs to be those of sarcoid, not a sarcoid-like lesion, yet most of the discussers favored necrobiosis as the most likely diagnosis.

DR. EUGENE TRAUGOTT BERNSTEIN: In necrobiosis lipoidica diabeticorum fat droplets are able to penetrate through damaged walls of the blood vessels by diapedesis into the cutis. These extracellular fat droplets, stained with sudan III, are imbibed into the tissues, causing necrosis. The disease has nothing to do with diabetes. In some instances it is a sequel of hypercholesteremia or some other variety of hyperlipoidemia. In necrobiosis lipoidica diabeticorum one does not find Masson's cells (epithelioid nevus cells of Merkel-Ranvier).

DR. ABRAHAM WALZER: With regard to the case presented last month, the histologic examination, I understand, has definitely shown the lesion to be sarcoid and not sarcoid-like. The disease must therefore be accepted as sarcoid and not necrobiosis.

Chronic Lymphangitis. Presented by DR. ABRAHAM WALZER.

B. F., a widow aged 47, is presented from the dermatologic clinic of the Jewish Hospital of Brooklyn. She gave a history of having had scarlet fever with renal and aural involvement at the age of 8 years, meningitis at 12 and a number of attacks of pneumonia. Her right ear was still discharging, and she was completely deaf on that side. About sixteen years ago she had "toxemia of pregnancy," and her blood pressure at that time was over 300 systolic. About four or five years ago she had a "tumor" removed from the roof of the mouth.

The present infection began about seven or eight months ago. The central part of the face and the right upper eyelid suddenly became red and swollen, accompanied with a slight rise in temperature (99.5 to 101.5 F.). This lasted for a few days and then gradually subsided. These attacks would recur every week or two, but the recession was never complete.

On Aug. 11, 1943, the patient was admitted to the hospital and after a thorough investigation was discharged in two and a half weeks with a diagnosis of chronic glomerulonephritis. There was no improvement in the lesion of the face.

At present the nose, the cheeks and the chin are swollen, indurated, faintly red and somewhat tender. The erythema is not sharply outlined. The upper eyelid is swollen but is soft and erythematous.

The patient also has a mild stomatitis with leukoplakia-like spots. The roof of the mouth shows a mild abrasion at the site where the "tumor" was removed. She has no teeth and wears upper and lower dentures. She also presents lesions of perlèche at both labial commissures.

DISCUSSION

DR. LOUIS CHARGIN: This seems to me to be a case of so-called habitual erysipelas, a recurrent form of this disease often associated with lymphangitis. There is evidently a focus of infection in the nose or the mouth, and something acts to start a new attack every so often. I think that this would be an excellent case for a thorough trial of penicillin therapy. If the infection is not controlled, a solid edema of the face is likely to develop.

DR. DAVID BLOOM: I agree with Dr. Chargin. When solid edema has developed, no medication is of any benefit. In this case there is a chance to prevent solid edema.

DR. EUGENE TRAUGOTT BERNSTEIN: I believe penicillin should be given to a total of about 1,000,000 units, in a dosage of 25,000 units every three hours.

DR. ABRAHAM WALZER: It has been suggested that this is a case of erysipelas. The absence of the crimson-red color, a smooth shiny glazed surface and a high temperature, all speak against erysipelas. However, the recurring attacks of solid edematous swelling, which never recedes completely but is progressive and permanent, speaks more for a recurring lymphangitis or a solid edema of the face.

Urticaria Due to Cold. Presented by DR. ABRAHAM WALZER.

T. F., a married woman aged 44, is presented from the dermatologic clinic of the Jewish Hospital of Brooklyn. There is no history of atopy. The patient had an appendectomy twenty-five years ago and "neurasthenia" ten years later for four years. About two and a half years ago she had a number of attacks of "Ménière's disease."

The present ailment began suddenly about ten years ago. The patient noted that on exposure to cold in the winter her face and her hands swelled and became red and itchy. This persisted for about fifteen to thirty minutes after exposure. Cold drinks or ordinary bathing in cold water did not affect her, but bathing in the sea would induce dizziness and fainting spells.

Complete physical and hematologic examinations and a urinalysis revealed nothing abnormal. The Wassermann reaction of the blood and also that of the spinal fluid were negative.

When an ice cube is placed on the skin of the forearm for two or three minutes, the skin becomes red and in about another minute a pronounced wheal forms, assuming the shape of the cube of ice.

DISCUSSION

DR. CHARLES WOLF: There is no doubt that this is a rather classic case of physical allergy, and one does not frequently see such a straightforward cause and effect phenomenon. Since Dr. Walzer attacks dermatologic diseases from the allergic standpoint, it would be interesting to have him tell the members how he expects to secure a therapeutic effect in this patient.

DR. LOUIS CHARGIN: If this patient is not much disturbed by the disease, I think it best to institute no treatment. However, if necessary, an attempt should be made to desensitize her to cold. Such desensitization has been reported in the literature. Histamine phosphate in these cases is without effect. It does not matter in what manner it is employed.

DR. EUGENE TRAUGOTT BERNSTEIN: I agree with Dr. Chargin that in physical allergy, particularly to cold, desensitization by gradual adaptation to cold plays an important part. It is known that exposure to cold produces swelling of the lips and the tongue, lacrimation, coughing and so forth. Cold anaphylaxis may cause death while one is bathing, as was pointed out by Horton. The subject elicited much attention in the literature (Horton, B. T.: *Proc. Staff Meet., Mayo Clin.* **2**:276, 1927). A sudden onset of urticaria due to cold makes bathers so helpless that they can hardly be rescued from drowning. The loss of consciousness is the sequel of cerebral edema resulting from the same mechanism as does the temporary loss of vision.

DR. ABRAHAM WALZER: The term "physical allergy" has been employed to describe these types of cases—a hypersensitiveness to a physical force, such as cold, heat and sunlight. The term, however, is not a good one because allergy denotes a reaction between chemicals. Nevertheless, the constant and frequent use of this term justifies its employment for hypersensitiveness to such physical forces.

With regard to treatment for urticaria due to cold, nothing has as yet been found to be a cure in these cases. In line with the procedure by which patients are desensitized to proteins by frequent and progressive administration of minute quantities of the offending antigen, it has been suggested that a similar course be followed in respect to allergy to cold. Bathing in cold water the temperature of which is gradually and progressively reduced has been tried but with no success. The sensitivity to physical forces apparently simulates the sensitivity to drugs in which desensitization cannot be accomplished by administering the drug in minute doses over a long period. Histamine phosphate has been injected in these cases, on the theory that histamine is released at the site of the wheal induced by cold and is the direct cause of the reaction. The injected drug is therefore supposed to desensitize the patient to histamine, but in practice this does not occur.

It is a purely theoretic supposition that in urticaria due to cold the cold releases "allergens" and that antibodies to these allergens are formed which can be passively transferred. While reports of experiments demonstrating this do appear in the literature, the majority of attempts to repeat these experiments have failed. In the division of allergy of the Jewish Hospital in Brooklyn, passive transfer of immunity to heat or cold has not been successful in a single instance, after many attempts over a long period.

DR. EUGENE TRAUGOTT BERNSTEIN: Nineteen cases have been reported in which it was possible to demonstrate the presence of an antigen-antibody reaction by means of passive transfer tests. Among those reporting are: E. Lehner (*Zentralbl. f. Haut- u. Geschlechtskr.* **41**:199, 1932), E. Liebner (*Zentralbl. f. Haut- u. Geschlechtskr.* **34**:406, 1930), F. Bernstein (*Dermat. Ztschr.* **64**:242, 1932), J. Affolter (*Schweiz. med. Wchnschr.* **63**:841, 1933), E. C. E. Bodenstein (*Zentralbl. f. Haut- u. Geschlechtskr.* **52**:364, 1936) and other investigators.

Dermatitis Medicamentosa (Fixed Eruption Due to Arsenic). Presented by DR. ABRAHAM WALZER.

A. H., a Negro woman aged 55, presented from the dermatologic clinic of the Jewish Hospital of Brooklyn, complains of an eruption on the body and in the mouth.

There was no history of syphilitic infection. About four years ago, during the course of a general examination, a positive Wassermann reaction of the blood was found, and the patient has since been treated at a local clinic with an arsenical and a bismuth compound. About fifteen months ago, after she had received approximately thirty injections of a bismuth compound and twenty injections of neoarsphenamine, it was noted that after an intravenous injection of neoarsphenamine "sores" developed in the mouth and raised red edematous pruritic lesions on the body. These would subside in three or four days and leave pigmented spots, only to recur at the same sites after every subsequent injection of the arsenical. This drug was discontinued about one year ago.

The patient shows scattered dark blue or black pigmented round or oval patches varying in size from that of a dime to that of a dollar or larger. They are sharply outlined and not elevated. Most of the lesions are on the upper part of the body.

A urinalysis, blood counts and a complete physical examination revealed no abnormality. The Wassermann reaction of the blood was 4 plus.

DISCUSSION

DR. LOUIS CHARGIN: I think that one is dealing with a fixed eruption due to the arsphenamines. This patient will probably be found sensitive to all arsphenamines, less so, perhaps to oxophenarsine hydrochloride than to the others. Fortunately this patient shows no lesions on the face, and treatment with the arsphenamines should be avoided if possible to obviate such an occurrence. It would be of interest to determine whether she is likewise sensitive to antipyrine and phenolphthalein—in other words, whether she shows polyvalent sensitivity.

DR. OSCAR L. LEVIN: Fixed eruptions from arsphenamine were formerly common. These are not observed so frequently nowadays, and I have not observed any in private practice in the past few years. About twenty years ago there was a patient at the Cornell Clinic who would show an exacerbation of a fixed eruption after each injection, and after seven or eight the use of arsphenamine was stopped and silver arsphenamine was given instead, without the production of an eruption. I agree with Dr. Chargin that it is not advisable to endanger a patient by the continued use of arsenicals when a patient who is not in the infectious stage presents a fixed eruption.

DR. ABRAHAM WALZER: The question of polyvalent sensitization in patients with a drug sensitivity is an interesting one, and it is not rare. However, one must bear in mind the fact that not infrequently the rash due to a specific drug may be reproduced nonspecifically by the ingestion of another drug and also by physical and mental states during the interval immediately following the recession of the drug rash. However, after the rash has been gone for some time, these nonspecific factors will not produce it again.

Urticaria Pigmentosa. Presented by DR. JESSE A. TOLMACH.

S. B., a man aged 52, born in Poland, employed as a dress operator, has had a cutaneous eruption for the past four or five years. This began on his abdomen and spread rapidly to other parts of his body. There is only slight itching at times. No one in the patient's family has had a cutaneous eruption as far back as he can remember. He has been suffering for a number of years from disease of the gallbladder. A cholecystectomy was performed in 1941. A right inguinal hernia developed several years ago.

The skin of the trunk, the shoulders, the arms, the buttocks and the thighs presents a generalized eruption consisting of multicolored macules, ranging from brownish to yellowish to slate-colored stains. On friction by hand or from tight clothing, the lesions turn into papules which may assume the size of large welts. The lesions predominate on the trunk and the shoulders, are vast in number and are arranged according to cleavage.

The urine was normal, and the Wassermann reaction of the blood was negative. The blood count showed 4,000,000 erythrocytes and 9,600 leukocytes, with 47 per cent neutrophils, 21 per cent monocytes, 30 per cent lymphocytes and 2 per cent eosinophils.

Biopsy performed by Dr. Sachs showed with the hematoxylin and eosin stain that the vessels of the middle and upper parts of cutis were dilated and there was a sparse, small, round and wandering connective tissue cell infiltration. Considerable edema was present throughout the cutis. The overlying epidermis showed no important change. There was a pronounced increase in the number of mast cells. The microscopic diagnosis was urticaria pigmentosa.

DISCUSSION

DR. JOEL SCHWEIG (by invitation): The question of the causal relationship between chronic disease of the gallbladder, hepatic damage and urticaria pigmentosa is interesting and deserves further investigation. Whenever the patient experiences pressure and tightness due to clothing, corresponding swelling and itching result.

DR. OSCAR L. LEVIN: I agree with Dr. Schweig that there may be a relationship between disease of the gallbladder and the liver and urticaria pigmentosa. I have frequently observed such a relationship between disease of the gallbladder and the liver and urticaria, angioneurotic edema and allied diseases. The reactions may be due to a decrease in the detoxifying action of the liver or possibly to the presence of an infection or a toxin in the gallbladder. In every case of urticaria or urticaria pigmentosa an investigation into the history of disease of the gallbladder should be made. I have also observed excellent results in urticaria following lavage of the gallbladder.

DR. DAVID BLOOM: As in young children, so in adults urticaria pigmentosa must be considered a nevoid eruption. The presence of disease of the gallbladder may be considered as coincidental.

DR. OSCAR L. LEVIN: In the young, one should also bear in mind the possible association of an eruption with a disorder of fat metabolism and the possible relationship to disease of the liver.

DR. CHARLES WOLF: It is commendable to project theories on cause and effect in disease, but it would be difficult to prove that there is a relationship in this case in view of the fact that disease of the gallbladder is a common affliction. In the course of a year several thousand patients are operated on in the city of New York for disease of the gallbladder and associated diseases of the liver. The members, as dermatologists, know that urticaria pigmentosa, both the juvenile and the acquired form, is a rare disease; the cases seen in the lifetime of any dermatologist are few. One cannot accept flimsy theories as an explanation of a disease as mysterious as urticaria pigmentosa. It is a mast cell formation having to do with the reticuloendothelial system. Many hemopoietic organs may be involved in the causation of the disease.

DR. ABRAHAM WALZER: I think that urticaria pigmentosa is being confused with chronic urticaria. There is no fundamental connection between the two. Urticaria pigmentosa is not urticaria, and the term is therefore a misnomer. The only resemblance, and it is a slight one, is the dermographia present in urticaria pigmentosa. Otherwise, both clinically and histologically, they are decidedly different entities. Urticaria pigmentosa is not an allergic manifestation and has no relation to food or any other antigen. As far as is known, it has no relation to disease of the liver or the gallbladder or to any focus of infection. In the infantile form it resembles a nevus more than anything else.

DR. JOEL SCHWEIG (by invitation): It is true that urticaria pigmentosa is not an urticaria in the true sense of the term, or an urticaria with pigmentation; it is a definite, separate entity capable of producing welts as seen in ordinary urticaria. Although the etiologic factor of urticaria pigmentosa is unknown, observations have been made in cases of urticaria pigmentosa that the manifestations were associated with hepatic damage. Our case reveals this relationship distinctly, as the urticaria pigmentosa appeared shortly after the first symptoms of the disease of the gallbladder became manifest. Of course, it might be coincidental. The argument that one does not frequently observe urticaria pigmentosa in association with disease of the gallbladder and that there is therefore no connection between the two is not valid, as one rarely sees diabetes associated with necrobiosis lipoidica, for instance, and yet nobody will deny the interrelation of the two diseases.

Roentgen ray therapy is being advocated for urticaria pigmentosa, but the benefit is limited. The eruption is known to have cleared spontaneously.

Dermatitis Lichenoides Chronica Atrophicans (Csillag). Presented by DR. OSCAR L. LEVIN.

E. F., a married woman aged 50 and a native of Puerto Rico, whose occupation is that of housewife, entered the Mount Sinai Hospital clinic one week ago complaining of an eruption of eighteen months' duration. She stated that white spots first appeared on the skin of the chest and spread to the shoulders.

On the right side of the chest are seen discrete small whitish polygonal flat atrophic papules. On the left side there are similar lesions and also others which show a tendency to become confluent and form patches. The centers of many of these show patent empty follicular orifices. There are also follicular scaly plugs. On the back are similar lesions, which show more prominence of the follicular plugs and which on palpation impart a nutmeg grater sensation. On the mucous membrane of the left labium majus there is a white flat pigmented plaque showing several small depressions, probably the result of papules similar to those observed elsewhere.

Biopsy specimens were taken from lesions on the chest, but as yet there has been no report.

DISCUSSION

DR. DAVID BLOOM: The appearance of the eruption is that of lichen sclerosus et atrophicus of Hallopeau. The characteristic follicular plugs are present in younger lesions and atrophy without plugs in older lesions.

Harry C. Saunders, M.D., *Chairman*

Frank Vero, M.D., *Secretary*

March 6, 1945

Dermatitis Medicamentosa (Iodide). Presented by DR. EUGENE F. KELLEY.

T. C., an Italian-born man aged 46, is presented from Vanderbilt Clinic with an eruption of the face, the neck, the trunk and the extremities of six years' duration. A squamous cell epithelioma of the lip is undergoing treatment.

In 1917, while the patient was in the Italian army, a penile lesion developed, and there was a positive Wassermann reaction of the blood. He received intramuscular injections of mild mercurous chloride and later a preparation of bismuth for a period of one year. After a four year interval treatment was resumed sporadically, consisting of a preparation of bismuth given intramuscularly. Seven years ago, in this country, intravenous treatment was begun and received at irregular intervals for a year. Six years ago a series of intravenous injections was given and also iodides in capsule form. Shortly after this medication was started abscesses and boils began to appear on the body, the face and the extremities. He took in all about 100 capsules over a period of three months. He stopped taking them when dizziness and heartburn appeared and the abscesses increased in number.

On the face, the neck, the trunk and the extremities there are numerous irregular, oval and round pigmented and depigmented scars distributed bilaterally. There are some active lesions on the trunk and on the cheeks consisting of follicular papules and small furuncles. There is a large scar on the back of the neck, the result of a carbuncle.

The urine was normal except for the presence of albumin (1 plus). The Wassermann and Kline reactions of the blood were negative.

DISCUSSION

DR. A. BENSON CANNON: We thought that the case was of particular interest because of the large, irregular, deep scars, apparently with great loss of tissue, which I do not recall having seen before in dermatitis due to an iodide. I think that Dr. Kelley has demonstrated that they are due to iodides in that the man is appreciably better since treatment with the drug was discontinued.

DR. GEORGE C. ANDREWS: I was particularly interested in this man because of the epithelioma on the lower lip. He has been exposed to much sunlight. He has had a biopsy and irradiation, which accounts for the crusted appearance.

Behçet's Syndrome, Abortive Form (?) (Recurrent Aphthous Oral Lesions and Recurrent Genital Ulcerations). Presented by DR. HELEN O. CURTH.

E. O. C., a single woman aged 23, is presented from Vanderbilt Clinic complaining of lesions of the mouth and vulva which have occurred since childhood. The patient was born in New York city of Irish and French Canadian parentage, and has been under observation since 1942. She is next to the youngest of nine brothers and sisters. Three children died in early childhood. No other member of the family has a similar disease.

The patient has suffered from recurrent lesions in the mouth since childhood. Menstruation began at the age of 14. One year earlier she noticed the first vulvar lesions, and these have returned often since. At the beginning they appeared between menstruations, but lately they sometimes coincide with menstruation. Some attacks begin with chills. Temperatures around 101 F. may persist for a few days. The ulcerations heal with deep scars and destruction of the vulva. At the beginning of the attack a mucous discharge is discernible, and sometimes the inguinal nodes on the involved side are inflamed. In former years attacks were accompanied by severe pains in the left or the right calf. Lately the attacks of oral ulcerations have been so severe and frequent that the patient has not been free from them at all. The patient denies sexual relations. She has always been in good general health. She has never been absent from New York city for any length of time.

Physical examination reveals no significant abnormality. There is no enlargement of the lymph nodes. The eyes are normal. The tonsils are small and can hardly be considered foci of infection. Examination of the teeth in November 1944 showed the upper right central incisor and the lower right cuspid to be abscessed, but these have since been removed. The lips, the tonsils, the tongue, the soft and the hard palate, and rarely the buccal mucosa, are the sites of superficial or deeper tender erosions which are covered with an exudate and surrounded by a red halo. The ulcerations show a deep, dirty base. Scars of healed ulcerations are seen on the tongue, the lower lip and the soft palate.

The vulva is the site of an extensive, indurated, atrophic and destructive process. Both labia majora show extensive scarring. The posterior part of both labia majora was removed in a plastic operation (1942), and a biopsy was made of the tissue. Both labia minora are enlarged and show multiple fenestration. When an ulceration is present, it shows in the early stage a large, necrotic area surrounded by a hemorrhagic border. Later a deep ulceration is seen which may measure 2 cm. in diameter. The base of the ulcer is granulating, and the border is infiltrated.

The uterus is slightly retroverted, and the small adnexa are not felt. The cervix was found on one occasion to be clear, and at another to show an erosion.

The laboratory examinations revealed no albumin or glucose in the urine. Repeated Wassermann and Kline tests elicited negative reactions. The number of white blood cells ranged between 11,850 and 15,900, with hemoglobin 92 per cent and red blood cells 4,850,000. Polymorphonuclear leukocytes were 72 per cent, small lymphocytes 22 per cent, large lymphocytes 5 per cent, and mononuclear cells 1 per cent. The sedimentation rate was 35 to 40 mm. per hour. Blood cultures during the patient's stay in the hospital showed no growth, nor did nose and throat cultures. The results of blood agglutination tests for Eberthella typhosa O and H and for Salmonella paratyphi A, B and C were negative. Results of Frei and Ducrey tests were repeatedly negative. Old tuberculin tests in a dilution of 1 : 10,000 elicited negative reactions.

Bacteriologic examinations of the genital lesions, including dark field examinations, scrapings for Donovan bodies and smears for chancroid bacilli and inclusion bodies, were negative. Slides and cultures for fungi were negative, as were repeated inoculation tests. Smears for gonococci from the cervix and an ulceration were negative. Bacillus crassus was once seen in great numbers in a smear from the genital lesion, but was not seen in the biopsy specimen. In a culture hemolytic Staphylococcus aureus and Staphylococcus albus, but no anaerobes, were found.

No inclusion bodies or Bacillus crassus were seen in smears from the oral lesions. Staphylococcus aureus, Staphylococcus albus and streptococci were found on culture.

Suspensions in saline solution were made from genital and oral scrapings. The suspensions were inoculated into mice, guinea pigs, cotton rats, embryonated hen's eggs and chick embryo tissue cultures of the Li and Rivers type. There has been no evidence of the growth of any viral agent.

The course and treatment were as follows: In May 1942 a plastic operation of the vulva was performed in the Sloane Hospital for Women. For a while afterward the patient had no recurrence of the genital lesions. Later the lesions began to recur fairly often. She was successively treated with 3 per cent sulfathiazole ointment, potassium permanganate soaks, and estrone cream locally to the genitals, and with hydrogen peroxide, analgesic tablets and estrone cream locally in the mouth.

General treatment consisted of injections of liver extract, nicotinic acid 100 mg. twice daily, sulfathiazole internally (2 Gm. daily for six days) and penicillin 1,710,000 units (given at the Presbysterian Hospital) and removal of two abscessed teeth. The patient has avoided brushing her teeth for several weeks, and has eliminated chicken, eggs and oatmeal from her diet.

All of these therapeutic attempts were given up when the impression was gained that the condition got worse rather than better. While the patient was receiving penicillin, especially, the extent of the oral lesions was larger than ever.

Biopsy of a genital ulcer showed granulation tissue at the base of the ulceration. The tissue was swollen and edematous. Areas below the ulcer were the site of a chronic inflammatory reaction with aggregation of polymorphonuclear leukocytes, lymphocytes and plasma cells. The infiltration was not found in any significant distribution around the blood vessels, which appeared thickened. Giemsa stains did not reveal the presence of any organisms. The diagnosis was genital ulceration of unknown cause.

DISCUSSION

DR. A. BENSON CANNON: I think that Dr. Curth dserves great credit for having called our attention to these cases. She has worked extremely hard on them, and has made a real contribution to the society and to dermatology.

DR. FRED WISE: Dr. Curth deserves great credit for calling our attention to cases of this syndrome. I believe that this is the second case she has presented. Many diseases are characterized by lesions involving the vulva and the mouth, sometimes coincidentally and sometimes separately, and, aside from Bacillus crassus, bacteriologic findings have for the most part been negative. Many observers believe that a virus is the causative agent. It will require much more invesigation to reveal the cause of these ulcerations. I hope that Dr. Curth will be successful in this field of investigation and will tell us more about the causation.

DR. GEORGE C. ANDREWS: One feature is the chronicity, as these cases run on for so many years. The classification is difficult, because it is hard to know where ulcus acutum vulvae ends and Behçet's syndrome begins, as many cases of ulcus acutum vulvae have been accompanied by oral lesions. The question is whether those cases of both oral and genital lesions were formes frustes of Behçet's syndrome. I happened to see in my office today a young woman with ulcerations similar to those presented by this patient. About five years ago she had extensive ulcerations in the vulva; sulfanilamide helped her so that she did eventually get entirely well, but she came in today with sores on her vulva again. She has had the condition for many years. We had a case of Behçet's syndrome at Presbyterian Hospital a while ago which was reported in the ARCHIVES OF DERMATOLOGY AND SYPHILOGY after presentation before the New York Dermatological Society. The patient had the disease for about ten years, with sores on the penis, iritis, conjunctivitis and blepharitis. He had subungual abscesses which were different from ordinary ones in that they would disappear after a few weeks by themselves. He also had ulcers in the mouth. The disease began with hydrops of the right knee joint, which is one of the common symptoms of Behçet's syndrome.

DR. MABEL G. SILVERBERG: I should like to suggest the use of smallpox vaccination. I had a case of chronic ulcers of the tonsil and buccal mucosa; the patient was vaccinated, a violent reaction occurred, and the lesions cleared up in forty-eight hours and have not recurred.

DR. HELEN O. CURTH: The question of Bacillus crassus is a perplexing one. This case does not differ from Lipschütz' original description of ulcus vulvae acutum. One of his cases was also accompanied by oral lesions, which he thought was coincidental. Since then, most observers have found B. crassus in genital lesions but have been unable to find it in the oral lesions. Matras, however, found B. crassus in the oral lesions. He, Samek and Fischer also obtained positive blood cultures. It seems to be the opinion of other observers that B. crassus would be found in the genital tract of many women, whether they have these ulcerations or not. The fact that men have the same kind of genital and oral lesions would also speak against the etiologic role of B. crassus. I called this case an abortive form of Behçet's syndrome because I was impressed by the similarity of the oral and genital lesions with those seen in cases of the fully developed syndrome. It may take twenty years before ocular lesions develop. I am thankful for the suggestion of smallpox vaccine and will try it. With regard to ocular lesions, one should insist on a picture of iritis, iridocyclitis or uveitis with hypopyon. I consider that the form of ocular lesion seen in this syndrome.

Moniliasis. Presented by DR. JAMES LOWRY MILLER.

R. V., a girl aged 7, is presented from Vanderbilt Clinic with an eruption of the scalp, the mouth and the finger nails of two and one-half years' duration. The patient was admitted in August 1942, complaining of red, crusted lesions involving the face and the scalp which had been present for two months. Examination at that time showed the entire scalp to be covered with a heavy crust, with many bald areas interspersed with clumps of hair. Perlèche lesions were present at the corners of the mouth, and red, pea-sized papular areas covered with crusts were present on the chin and the forehead and around the nose. Both thumb nails were dystrophic.

On the scalp there are many red, bald areas between which are areas of normal scalp. A number of the red areas are covered with thick, adherent crusts. No scarring is seen. On the forehead there are a few pea-sized, red, crusted papules. The corners of the mouth are red and covered by a white, lacy pellicle which extends back on the mucous membrane of the mouth. The left first and third and the right index finger nails are dystrophic with chronic paronychia at their bases.

General physical examination revealed no abnormality except that the child is pale and somewhat underweight. Cultures from the scalp, the finger nails, the mouth and the feces were all positive for Monilia albicans. The complete blood count was normal.

Treatment has consisted of undecylenic acid, sodium propionate, methylrosaniline chloride, salicylic acid, injections of crude liver, and many other remedies. Methylrosaniline chloride (gentian violet) has been the most efficacious remedy, and one nail and accompanying paronychia have cleared under treatment with fuming nitric acid.

Moniliasis. Presented by DR. JAMES LOWRY MILLER.

E. R., a white man aged 25, was admitted to the Vanderbilt Clinic on August 8, 1944, suffering with a generalized dermatitis which has been present since he was 3 months old. It began in infancy on the buttocks and gradually spread to involve most of the body. It was treated as an infantile eczema, and at the age of 5 all lesions completely disappeared, and he remained clear for one year. Since that time cutaneous lesions similar to the presenting eruption have existed at all times. He has never had any intesinal or respiratory symptoms. During the last year he has noticed loss of hair from the scalp and the eyebrows. The toe nails have been involved for years, and the finger nails more recently have shown changes.

Large infiltrated erythematous scaly patches varying from pea size to palm size are scattered over the entire body, including the hands and the face. On

the scalp there are a number of similar patches. The hair on the entire head is thin, but no atrophic areas are present. The finger nails are dystrophic, particularly at the sides. There is no paronychia. Perlèche lesions are present at the corners of the mouth. On the mucous membranes at the side of the mouth and on the tongue there are white, lacy pellicles.

Cultures were positive for Monilia albicans from the feces, the sputum and the tongue. Repeated cultures from the nails, the scalp and the skin have been negative.

The Wassermann reaction of the blood was negative.

Sections of the cutaneous lesion disclosed acanthosis, hyperkeratosis and parakeratosis. Epithelial cells with eosinophilic cytoplasm were present. A chronic inflammatory reaction within the derma was seen. The diagnosis was chronic dermatitis.

A roentgenogram of the chest in the posteroanterior projection showed no evidence of recent parenchymal infiltration. Both costophrenic angles are clear. The tracheal air column appeared in the midline. The heart was not abnormal. Some calcium depositis were seen in both hilar regions.

DISCUSSION

DR. GEORGE M. LEWIS: I agree with the diagnosis. The clinical features are typical, and there is a positive culture. The question of therapy is one of the most difficult in dermatology, and the outlook as to the future must be reserved. Fortunately, these cases are rare.

DR. BEATRICE M. KESTEN: The habitus of patients with moniliasis is characteristic. This seems to make it impossible to combat the infection in either the skin or the intestinal tract. Even giving methylrosaniline chloride in capsules has not been effective.

DR. WILLIAM CURTH: The man has a brother with the same infection. Both have been seen here in years gone by, and reported by others (Satenstein, D.: Moniliasis, ARCH. DERMAT. & SYPH. **28**:124 [July] 1933; Lapowski, B.: Miliary Pustular and Erythematous, Squamous, Nummular Dermo-Epidermite in Progressing Centrifugal Plaques (Gougerot), ARCH. DERMAT. & SYPH. **30**:144 [July] 1934; **30**:308 [Aug.] 1934).

A Case for Diagnosis (Moeller's Glossitis? Glossitis Due to Vitamin B Deficiency? Glossitis Due to Phenobarbital? Presented by DR. WILLIAM CURTH.

F. C., a Rumanian woman aged 62, is presented from Vanderbilt Clinic with an eruption in the oral cavity of five months' duration. In October 1944 small blisters which ruptured after a few days appeared on the tongue and left the tongue sore. Her physician considered pemphigus and referred her to the Vanderbilt Clinic. Sodium perborate and sodium bicarbonate were applied without success. For about thirty years there have been occasional "canker sores" which have become more frequent since the teeth were removed twelve years ago and the patient began to wear dentures. She cleans them with Squibb's tooth paste. Her general health has been fairly good with the exception of some increase in the blood pressure, for which she has taken phenobarbital since September 1944. The menopause occurred at the age of 47.

The sides of the anterior half of the dorsum of the tongue show irregular, sharply defined red areas, neither elevated nor depressed, with a greatly thinned surface and an absence of papillae. The central portion of the tongue presents whitish papillae. The posterior papillae are not enlarged. Vesicular or bullous lesions were not seen during a period of observation of three weeks, in spite of continued phenobarbital medication.

Examination of the blood showed hemoglobin 102 per cent, red blood cells 5,150,000, white blood cells 8,700, polymorphonuclear leukocytes 59 per cent and lymphocytes 41 per cent. Examination of stomach contents after an Ewald test

meal showed total hydrochloric acid 84 degrees and free hydrochloric acid 80 degrees. Wassermann and Kline reactions of the blood were negative. Microscopic examination and culture for fungi were negative.

A biopsy specimen from the upper edentulous gum showed a pronounced hyperemia with an inflammatory exudate and edema in the corium. The epithelium of the basal cell layer was destroyed in many places, with desquamation at the sites of the destroyed epithelium. The diagnosis was desquamative gingivitis.

Daily applications of an estrone ointment resulted in considerable improvement of the condition of the gums and the tongue. She also received three injections of a liver extract, 6 units each, on February 14, 23 and 28.

DISCUSSION

DR. ISADORE ROSEN: I should be inclined to a diagnosis of drug eruption rather than Moeller's glossitis. Pain and the other features usually associated with Moeller's glossitis are entirely absent. The fact that the patient has been taking large doses of phenobarbital over long periods would tend to corroborate the diagnosis of drug eruption.

DR. CHARLES WOLF: If this is a manifestation of avitaminosis, I should like to know why estrone was applied to the gums.

DR. FRED WISE: In Jadassohn's "Handbuch," Moeller's glossitis is described as a symptom of pernicious anemia. In this patient no signs of pernicious anemia are present. The possibility of a drug reaction must be entertained in lesions of this kind, despite a negative personal history.

DR. A. BENSON CANNON: When this patient was first seen at Vanderbilt Clinic, several of us thought of syphilis and of phenobarbital. Dr. Rosen presented a case which was the exact counterpart of a syphilitic tongue, which it was thought to be until proved due to phenobarbital. I am pleased to hear tonight for the first time that the woman has been taking phenobarbital, and with Dr. Rosen's case in mind, I would not hesitate to attribute the condition of the tongue in this case to the use of that drug.

DR. WILIAM CURTH: This woman has been given injections of liver extract and has improved considerably. Our dental department performed a biopsy of the gum and suggested treatment with an ointment containing estrone, which was given her. The patient still suffers from hot flushes.

Urticaria Due to Cold (Improved with Histamine Injections). Presented by DR. J. GARDNER HOPKINS and DR. BEATRICE M. KESTEN.

D. G., a white woman aged 55, a Russian housewife, came to Vanderbilt Clinic on Feb. 13, 1940, complaining of itching and swelling of exposed areas when subjected to cold, dating from December 1939. While out in the cold the patient's face began to itch and felt numb. When she came indoors her face was swollen. Since then each time the patient goes out in the cold her face and extremities itch, and red blotches appear and then swell. After she comes into the warmth the symptoms subside in an hour or so. When cold water or ice touch the skin or even when the patient eats ice cream the mouth itches and burns, and the lips swell. There have been no hives from other causes.

The general health is good except for frequent headaches, often associated with being in the cold, hoarseness for the past year and arthritis.

Submerging the hands in water 20 C. or lower, or applying an ice cube to the skin for one minute produced redness, swelling and wheals which itched. Injection of histaminase or epinephrine previous to application of ice afforded no protection from hives when subjected to cold. Local contact with ice after iontophoresis with histaminase gave partial protection.

Intradermal tests with mecholyl and carbaminoylcholine were negative. Passive transfer tests for cold agglutinins were also negative.

The patient was given 15 to 60 units of histaminase a day orally for six weeks with no relief. From May 1940 to May 1944, except during the summer months,

the patient received an injection of histamine phosphate weekly or bimonthly. The initial dose was 0.001 mg. intracutaneously, and this was slowly increased to 0.4 mg. From October 1944 to date the patient has received an injection of histamine azoprotein weekly. The initial dose was 0.05 cc. given subcutaneously.

Since November 1944 the patient has had no hives. When the temperature reaches 10 C. to 15 C. her face tingles and feels tight, but there is no perceptible swelling. If the patient eats ice cream the tongue and lips prickle.

DISCUSSION

DR. MAURICE J. COSTELLO: I presented a case before the Manhattan Dermatologic Society about two months ago, in which the patient showed a similar picture. Every time she was exposed to cold air she experienced swelling of the cheeks, the eyelids, the hands and the ankles. The intradermal administration of small doses of histamine phosphate completely cured the disease in two months. If histamine is to be of use at all, it should be indicated in the physical allergies.

DR. GEORGE C. ANDREWS: Dr. Bernstein's ideas on passive transfer are not fully accepted—by Robert Cooke, for instance, who recently wrote an article in the *Journal of Allergy* stating that those examples of passive transfer in cold and heat allergies have not been fully substantiated, and he doubts that there are antibodies that can be passed on in these physical allergies.

DR. BEATRICE M. KESTEN: It is possible to accustom patients to cold by baths, by graded histamine injections, and by giving histamine orally—that is, by putting it on the mucous membranes of the mouth. It would seem that injection of a haptene (histamine plus globulin) is effective.

Ainhum. Presented by DR. FRANK VERO.

A. S., a Negro aged 60, is presented from Vanderbilt Clinic with a lesion of the right small toe of two years' duration.

The patient was born in Florida and lived in the Philippines from 1908 to 1911.

For the past two years the patient's right small toe has gradually become "pinched off" by a constricting band at the base. The process was completely painless until recently, when he began occasionally to have a "burning sensation" in and around the toe.

Examination shows the base of the right small toe to be constricted by a sclerotic ring. There is considerable maceration between the toes.

Microscopic examination of the toe nails was positive for fungus.

Calcification of Gluteal Regions Following Injections of Heavy Metals (Mercury). Presented by DR. F. PHILIP LOWENFISH.

L. F., a man aged 57, is presented from Vanderbilt Clinic with an affection of the buttocks which has been present for fourteen years. The patient has been under observation for treatment of syphilis since October 1928. Prior to this he had one hundred and fifty intramuscular injections of a preparation of mercury and one hundred intravenous injections of arsphenamine in the old Vanderbilt Clinic, three years before this date. In 1931 a pronounced induration of metal-like quality was noted over both buttocks. No lumps or nodules were felt. In 1928 the induration about the buttocks was unchanged, and the patient did not complain of any discomfort or pain. In January 1944 he began to suffer intense pain in the buttocks, and the area seemed much harder with lumplike and nodular masses, and it had become more extensive. Because of continuous pain the patient was referred to the surgical department for opinion and biopsy. A nodule was removed from the left buttock in February. He was treated in the physical therapy department with diathermy and static wave treatments to both buttocks. After six months this treatment was discontinued; there was little improvement. In January 1945 the pain was getting more intense, and

the patient complained of hardness and difficulty in sitting down, with the pain and induration extending up into the lumbar region. Because of osteoarthritis he was referred to the arthritis clinic a few days ago, where they felt that he was not a problem for them but suggested the fracture clinic for this type of pain referable to the low part of the back.

In 1931 a roentgenologic examination of the pelvis showed numerous streaky shadows of metallic density scattered throughout the region of the buttocks. The bones of the pelvis did not suggest abnormality.

In 1938 an anteroposterior roentgenogram of the pelvis showed an increase in the number of streaky shadows present in the region of the buttocks bilaterally since the examination of July 23, 1931. Otherwise there had been no significant change.

In 1944 a roentgenologic examination of the pelvis showed the presence of numerous streaky shadows of calcium density in both buttocks, indicative of previous administration of heavy metal. The bony structures of the pelvis appeared normal.

In January 1945 a roentgenologic examination of the pelvis and the spine showed no evidence of bone abnormality. The previously noted shadows of metallic density resulting from intramuscular heavy metal therapy were about the same in distribution and appearance. Osteoarthritis was seen in the lumbar spine.

In February anteroposterior and lateral views of the pelvis showed the previously described shadows of metallic density to be more numerous in this examination. In the anteroposterior roentgenogram they extended from the anterior superior part of the spine to the lesser trochanter. The bones of the pelvis did not suggest any abnormality.

The Wassermann and Kline reactions of the blood and the spinal fluid have been repeatedly negative since 1928.

In spite of the fact that no abnormalities were found on physical examination, and because of the patient's complaints of pain in his knees, legs and toes, and of impotence, weakness and nervousness, he has received small doses of arsphenamine and silver arsphenamine and iodides by mouth. This treatment was given at long intervals, and the patient says it "peps" him up and makes him feel better.

A nodule was removed from the left buttock in February 1944. The mass measured 2 by 1.5 by 1 cm. It was extremely hard and was covered with ragged, fibrous attachments. On attempting to cut the nodule it was found to be composed of material of calcium density. The cut surface showed it was composed of whorls of fibrous-like tissue alternating with whorls of stony hard, white, calcified tissue. It was not until October, eight months later, that the microscopic examination was reported. The tissue was extremely hard and required prolonged decalcification. This resulted in the disappearance of most of the few cellular elements which remained in the calcified mass. However, a few normal-appearing nerve and blood vessels running through the center of the mass could be made out. Dense bands of collagenous connective tissue were seen coursing through the tissue and surrounding the areas of calcification. The nature or cause of the calcification could not be determined, but the appearance of the tissue was compatible with the history of injection of heavy metals into the gluteal region, although none of the material could be made out in the specimen. The presence of nerve fibers within the mass, it was felt, could well account for the history of pain in this region. The diagnosis was calcification of the gluteal region (following injections of heavy metals?).

DISCUSSION

DR. G. F. MACHACEK: I am inclined to think that this is a real bone tumor, which I have seen in similar cases.

DR. ISADORE ROSEN: I agree with the diagnosis as presented. I have seen all kinds of infiltrations following the injection of the various insoluble prepara-

tions of mercury, but I have never seen such an extensive, hard, bonelike infiltration as this patient presents.

DR. F. PHILIP LOWENFISH: Injections of a preparation of mercury were given between 1925 and 1928, about one hundred and fifty in all.

Sarcoid (Healed) of Skin, Lungs, Bones, Larynx and Kidneys? Presented by DR. BEATRICE M. KESTEN.

C. R., a Negro woman aged 35, a domestic servant, born in New York city, is presented from Vanderbilt Clinic with an eruption of the face, the hands, the forearms and the right elbow of fifteen years' duration. The patient was admitted to Presbyterian Hospital on Nov. 3, 1937, for progressive cutaneous lesions which had been present for the previous seven years. The eruption began with acute pain and swelling of the distal phalanges successively and spread to the entire hands and lower aspect of the forearms. Four years ago pimples developed about the mouth and the nose and continued to envelop the orifices. Similar lesions developed about the eyelids ten months ago. Eleven months ago the patient began to complain of malaise, fatigue and cough, and she has recently become hoarse, and swelling of the ankles has developed.

Examination showed numerous discrete, erythematous, firm, slightly tender papules on the eyelids, the nose, the lips and the chin. In addition, there were deep erythematous nodules about the nares, covered with crusts. The fingers were spindle shaped and covered with nodules which were discrete, firm and slightly tender. These extended onto the backs of the hands and were scattered over the forearms and the right elbow. There was a stricture of the pharynx and destruction of the epiglottis; the cervical nodes were enlarged; the lungs were clear, the heart normal, the liver enlarged, and edema of the ankles was present.

In 1937 tests with old tuberculin elicited negative reactions in dilutions of 1:10,000 and 1:1,000. The sputum was negative for tubercle bacilli. A biopsy from the right nostril contained numerous tubercles composed mostly of epithelioid cells without necrosis. A guinea pig inoculated with a nodule from the nostril did not contract tuberculosis. Roentgenologic examination of the chest showed dense hilar shadows suggestive of bilateral hilar adenopathy. There were increased bronchovascular markings in the lower lung fields. Roentgenograms of the hands showed sharply circumscribed oval defects in the proximal phalanges and in some of the middle and distal ones. There was cystlike degeneration in the styloids and the fifth right and the first left metacarpal bone. The feet showed similar but less advanced changes. The rest of the skeleton was normal except for slight generalized decalcification.

The results of blood studies were as follows: The hemoglobin was 70 per cent, erythrocyte sedimentation rate 75 mm. in one hour. The serum protein was 8.9 cm. per hundred cubic centimeters; albumin, 3.7 Gm.; globulin, 5.2 Gm.; nonprotein nitrogen, 32 mg.; serum phosphatase, 32 Bodansky units; phosphorus, 2.8 mg.; calcium, 12 mg.; sodium, 127 milliequivalents; potassium, 4.5 milliequivalents; cholesterol, 338 mg.; chlorides, 590 mg., and carbon dioxide, 60.7 volumes per hundred cubic centimeters. There were 4,600 white blood cells with 11 per cent eosinophils.

The urine showed 1 per cent albumin, with a few granular casts.

The course and treatment were as follows: The patient was placed on a high protein, high caloric, high vitamin and salt-poor diet, with added cod liver oil and wheat germ, and was permitted only light work. The lesions on the nose were removed by desiccation. In November 1939 the serum phosphatase was 13.9 units, the cholesterol 213 mg. and the chlorides 612 mg. per hundred cubic centimeters. Roentgenograms of the hands showed no new lesions, the cysts in the styloids had disappeared and all of the foci appeared a little smaller, with the surrounding bone of better density. The lung fields were clear, and by May 1940 all the cutaneous lesions had disappeared.

In May 1940, reactions to tests with old tuberculin were negative in a dilution of 1:1,000,000 and positive in a dilution of 1:100,000 (1 cm. erythema with induration). Since May 1940 the tuberculin test has remained positive. A test with a dilution of 1:1,000 in September 1944 resulted in a bulla 3 cm. in diameter with a deep induration.

Reexamination of the chest in September 1944 showed it to be clear. Roentgenologic examination of the hands and feet in October 1944 showed no further change from 1939.

The skin has remained clear, there has been no edema of the ankles, but the patient remains hoarse.

Miliary Lupoid of the Face: Generalized Lichenoid and Eczematoid Dermatitis Resembling Mycosis Fungoides. Presented by DR. GERALD F. MACHACEK.

S. M., a Negro woman aged 33, is presented from Vanderbilt Clinic with a generalized eruption of four years' duration. This began as a few reddish macules on the left side of the chest and spread gradually to involve the entire body over a period of several months. At first there was no itching. The patient's private physician gave her injections in the hip and drops to take in water, but these were without benefit. She had no local treatment or roentgen irradiation before coming to the Vanderbilt Clinic. When healed, the macules left pigmented spots. The patient sought treatment at Vanderbilt Clinic in January 1944, and she states that she was somewhat helped by a series of roentgen irradiations, but otherwise continued to get worse. On July 14 she was admitted to Presbyterian Hospital, at which time the skin of the entire body, except the face, was involved. The eruption was a hyperpigmented, lichenified dermatitis with a tendency to bizarre contours. There was no oozing, but slight fissuring and maceration were seen between the toes. The hair of the scalp was thin, and a few patches of lichenification were noted on the scalp. The palms and the soles showed thickening and some pigmentation. There was a generalized adenopathy.

The patient's condition grew steadily worse in the hospital. Mild local treatment was given, with a course of typhoid injections, vitamin supplements and injections of crude liver. The skin of the axillas began to ooze, and the lichenified areas began to show infiltration. No gross abnormalities were noted in any studies.

Before the patient came to the hospital a biopsy specimen was reported as indicating psoriasiform dermatitis; another biopsy specimen taken from an infiltrated lesion on the back while she was in the hospital indicated "lymphoblastoma (mycosis fungoides)." Roentgen rays in fractional doses were then given to the entire body, in addition to the mild local treatment. The patient's condition improved slowly, and she was discharged in the fifth month of hospitalization, at which time the skin of the face and the ears was still oozing slightly. The biopsy specimen taken at this time from an area near the lower lip was reported as indicating "tuberculosis cutis."

The laboratory data were as follows: On July 16, 1944, hemoglobin was 11 Gm. (76 per cent). There were 3,500,000 red blood cells and 8,800 white blood cells. Neutrophils were 58 per cent; lymphocytes, 30 per cent; eosinophils, 7 per cent; monocytes, 4 per cent, and basophils, 1 per cent. On July 17 the blood arsenic was 0.02 mg. per hundred grams of dry blood. On July 19 the plasma vitamin C was 1.3 mg. per hundred cubic centimeters. On August 4 a roentgenologic examination of the chest showed no abnormalities. On September 29 there were 10,300 white blood cells. The neutrophils were 51 per cent; the lymphocytes, 41 per cent; the monocytes, 7 per cent, and the eosinophils, 1 per cent. On September 30 cultures from the lesions on the lids yielded hemolytic Staphylococcus aureus. On October 2 a roentgenogram of the chest revealed no abnormalities. On November 10 the hemoglobin was 12.8 Gm. There were 3,900,000 red blood cells and 9,650 white blood cells. Neutrophils were

70 per cent; lymphocytes, 18 per cent; monocytes, 4 per cent; eosinophils, 7 per cent, and basophils, 1 per cent. Reactions were negative to tests with old tuberculin, in a strength of 1:1,000,000 on November 10, of 1:10,000 on November 13 and of 1:1,000 on November 17. On November 29 the hemoglobin was 11.5 Gm. The neutrophils were 81 per cent; the lymphocytes, 13 per cent; the eosinophils, 5 per cent, and the monocytes, 1 per cent.

Five urinalyses revealed no abnormality. Tests for cutaneous allergy were performed but were not helpful.

DISCUSSION

DR. A. BENSON CANNON: This patient was first believed to have a generalized exudative type of dermatitis, especially because of the extensive exudation and crusting. On admission, routine roentgenograms of the chest disclosed active tuberculosis of the lungs, so much so that we thought that the patient should be isolated. The eruption changed, became lichenified, a melanoderma developed, and there were lichenoid patches and thickening of the soles and palms and persistent swelling around the eyes. It made us think of an arsenical dermatitis, and the blood did show about four times the normal content of arsenic. The patient was given calcium and sodium thiosulfate, injections of typhoid bacilli, irradiation and other remedies; nothing helped her a great deal. She had an acute exudative eruption of the side of the cheek and chin, and this we were unable to diagnose clinically. Dr. Machacek said that it finally showed characteristic tuberculosis histologically. I am wondering whether, on the basis of tuberculosis of the lungs and the skin, the condition could not fit into generalized exfoliative tuberculosis, rather than mycosis fungoides.

DR. MAURICE J. COSTELLO: On several occasions patients have been shown before this section who have had pityriasis rosea-like eruptions, or lichen planus, from the administration of the arsphenamines. The fact that there was an exacerbation of the pulmonary tuberculosis after the injection of arsphenamine would substantiate that opinion.

Chronic Lymphangitis and Chronic Recurrent Angioneurotic Edema of the Face. Presented by DR. F. PHILIP LOWENFISH.

L. S., a white man aged 45, is presented from Vanderbilt Clinic complaining of swelling of the face of fifteen years' duration. About fiifteen years ago, after and acute attack of erysipelas of the face which healed in about ten days, the upper lip was left swollen, and it has remained so since that time. The patient thinks that it gets larger and then smaller at times, but it has never even approached normalcy. The huge, boggy swelling hanging under the chin for the same length of time has apparently receded considerably during the past two months. About six weeks ago a pinkish edema of the upper right eyelid appeared, and this has remained fixed. The patient has had recurrent edema of the upper eyelids for many years. The upper lip is enlarged, thick and rubbery, and juts forward somewhat like the peak of a cap.

The laboratory data are as follows: Wassermann and Kline reactions of the blood were negative. A complete blood count and sedimentation rate were normal. Roentgenograms of the frontal, ethmoid and sphenoid sinuses were clear.

The patient has had twenty teeth extracted, including all from the upper jaw and a few from the lower jaw. A series of staphylococcus toxin injections has been given, and about three months ago he received a course of 1,280,000 units of penicillin given intramuscularly (20,000 every three hours for eight days). His condition has remained unimproved, and he is now receiving filtered roentgen ray therapy to each side and to the under surface of the upper lip. Up to the present time he has had six treatments given a week apart of 150 r each (65 kilovolts, 20 milliamperes, filtered through 2 mm. of aluminum and at a distance of 14 cm.).

The patient is presented for suggestions as to further treatment.

DISCUSSION

DR. ISADORE ROSEN: The only therapy that I can suggest is plastic surgery.

DR. MAURICE J. COSTELLO: We have treated at Bellevue Hospital a number of patients whom we cannot say were permanently cured, but who were certainly greatly improved while the sulfonamide drugs were administered. I think success is more likely to occur if the sulfonamide drugs are continued for a long period of time.

A Case for Diagnosis (Lipoidosis?). Presented by DR. PAUL GROSS.

N. I., a man aged 19, was seen at the Hospital for Joint Diseases because of an extensive cutaneous eruption which he had first noticed eight months ago. The first lesions to appear were nodes on his fingers. These increased greatly in size and number but caused no discomfort. Except for measles, there was no history of previous illness.

On the second, third and fourth fingers of the right hand and on the left index finger are nodules of a bluish red color and rather firm consistency. They are located near the finger joints, and the largest ones are about the size of a pea. They are freely movable and not tender. On the extensor surface of the forearms in juxta-articular position to the elbows there is a larger nodule, about the size of a cherry, subcutaneous and covered by normal skin. The entire pubic area is covered with reddish brown papules with a rounded top which shows slight scaling. These papules are the size of a large pinhead, densely arranged but not confluent, and form a pattern resembling a lichen moniliformis. There are many small, discrete, translucent papules of a yellowish pink color in both armpits and on the pinnae of the ears. There is an acneiform eruption on the chest and upper part of the back, and an erythema and minute papules in the nasolabial folds. A few whitish, flat, papular lesions are seen on the buccal mucosa corresponding to the last molar.

Roentgenograms of both hands revealed moderately advanced arthritic changes in the interphalangeal joints. Circular defects were present in the juxta-articular ends of the small bones, suggestive of gout. There were also arthritic changes in both wrist joints. The lateral views of the elbow joints were radiographically normal.

There was no albumin or sugar in the urine. The Kahn and Kline reactions of the blood were negative. A blood count revealed no pathologic changes. The sedimentation rate was 8 mm. in forty-five minutes. A blood chemistry study showed 93 mg. sugar per hundred cubic centimeters and a total cholesterol of 102 mg. per hundred cubic centimeters, of which 32 mg. was free cholesterol.

DISCUSSION

DR. FRED WISE: If I am not mistaken, only 4 or 5 bona fide cases of extracellular cholesterosis are described in the literature of today. No special stains for fat were made in this case, but if sections were properly stained for fats, the histologic picture of extracellular cholesterosis might be demonstrated in sections from one of the lesions on the hand.

DR. EUGENE T. BERNSTEIN: In my opinion the diagnosis can readily be made on clinical grounds, particularly on morphologic attributes. I have no doubt that a histologic examination would confirm the diagnosis. The lesions seen on the patient show transitional shades from chamois yellow through brown to a dusky red. On the left ear one could see the typical chamois hue of xanthoma. On the elbows the lesions have a brownish discoloration, whereas the lesions on the hands are dusky red. It seems to me that we are dealing with a metabolic disturbance of lipoids, a picture similar to that described in extracellular cholesterosis. Tannhauser, an authority on lipoid metabolism, thinks that the designation of extracellular cholesterosis should be disregarded and replaced by the more embracing diagnostic term, lipoidosis. This case presents an example of such an instance.

DR. PAUL GROSS: On clinical grounds, we were in favor of the diagnosis of extracellular cholesterosis. The case reminded us of a patient presented by Dr. Oscar Levin before this section, who showed a similar array of lesions. At that time Dr. Bernstein doubted this diagnosis. The pathologic findings of the sections obtained by biopsy from the skin of the pubic region in this case make it difficult to maintain the diagnosis of extracellular cholesterosis. The presence of many giant cells deviates from the description given by Urbach. The results of stains for fat should decide whether we are dealing with an unusual type of lipoidosis. The low total cholesterol in the blood of our patient resembles the findings in Urbach's case, except for the normal ratio of free and esterified cholesterol in our case.

NOTE.—On the basis of several biopsies, the diagnosis of lipoidosis can be ruled out. The histologic changes are so unusual that a definite diagnosis cannot be offered at present. The sections were studied by Dr. Jaffe and Dr. Lichtenstein and were examined by Dr. Machacek, and the description of the pathologists was as follows:

A specimen obtained from the skin of the pubic region showed that the epidermis was atrophic in the affected areas. In the cutis one observed vascularization, clumps of peculiar foreign body giant cells and collections of small mononuclear cells dispersed around vascular channels. A second specimen from the same region showed some fibrosis in the subpapillary zone of the corium, increased vascularization and the presence around some of the vessels of chronic inflammatory cells. There were occasional giant cells, present, but not nearly as many as were seen in the previous specimen. A sudan stain showed the presence of lipid within some of the connective tissue cells, but on the whole the lesion contained comparatively little lipid.

Sections of an extirpated nodule on the fingers showed essentially the same process. Within the superficial and deeper layers of the cutis there were collections of cells apparently of the nature of leukocytes, and numerous multinuclear giant cells. There was evidence to suggest that these cells were derived from the reticuloendothelial cells of blood vessels. There was no appreciable amount of lipid in the lesion as seen in sudan stain, and chemical analysis of a slice of tissue likewise failed to reveal any lipid. In another lesion there were observed conspicuous collections of blood vessels, considerable fibrosis and also a partial infarction.

A Case for Diagnosis (Nevus?). Presented by DR. LOUIS CHARGIN.

A. B., a man aged 24, had an eruption of the left side of the face some six years ago. The eruption spread rather rapidly, so that in a space of several months it extended to the present dimensions. He has been treated by several physicians with local remedies without the slightest effect. The patient has diabetes, takes insulin and is under good control.

Occupying the left cheek, the left ear, the jaw and the adjacent neck there is a papular eruption which is irregularly distributed over the affected areas, the border being irregular in outline. It is dark red, slightly scaly in part, but mostly smooth and shiny. Superficial examination gives the impression of lupus vulgaris, but on diascopy there is no suggestion of tubercles nor is there any reason for a diagnosis of lupus erythematosus. There are no subjective symptoms.

Biopsy showed the epidermis to be considerably acanthotic, with the palisade layer intact. The surface was verrucous, covered by a densely laminated horny layer. In the subepidermic region the vessels were dilated, and about them was a moderate small round and wandering connective tissue infiltration. There was a slight increase in mast cells, but not enough to make a diagnosis. The elastic tissue was unchanged. There was no evidence of epithelioid cells or of tubercles,

and no evidence of lupus vulgaris. It was felt that the picture might possibly fit in with a nevus.

DISCUSSION

DR. A. BENSON CANNON: I could not make a better diagnosis than Dr. Chargin's, but I don't know that I should have thought of nevus either from the clinical appearance or from the age of the patient. I have never seen a nevus develop in a man 20 or older, and I believe he has had the lesion only six years. I had occasion to look up the literature, and the oldest patient whom I found was 13 when the nevus developed. I should think from the lesions on the scalp and face that it might be explained as psoriasis, although the histology has no resemblance either to psoriasis or to nevus.

DR. FRED WISE: A diagnosis of nevus is hard to accept because of the diffuse, widespread scaling eruption on the entire scalp. If one examined the scalp alone the thought of nevus would not occur. The scalp lesion resembles psoriasis or seborrheic eczema, but the presence of a linear lesion on the nose and the sharply bordered lesion on the neck lead one to consider a nevus or a nevoid disease.

DR. CHARLES WOLF: One cannot be overinfluenced by the biopsy report here, but on clinical grounds there are enough objective signs to consider it in the group of a psoriasiform eruption. The clinical data supporting the diagnosis are these: First, there are sharply demarcated lesions in the scalp with normal skin interrupting the affected areas. There are micaceous, silvery scales which could be removed, eliciting pinpoint hemorrhages. Furthermore, the man has stippling of one of the nails. It is well known that psoriasis may for many years be represented by a solitary lesion. As time goes on, other lesions may develop. I would therefore tentatively say that it is psoriasis. The biopsy revealed acanthosis, which is one of the definite features of psoriasiform pathology.

METROPOLITAN DERMATOLOGICAL SOCIETY

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Feb. 19, 1945

Unilateral Acrodermatitis Chronica Atrophicans. Presented by DR. GERALD FRANK MACHACEK.

H. W., a white woman aged 50, began to have lesions following sunburn five years ago which now involve the right forearm and part of the right arm throughout most of the circumference. These are erythematous, atrophic and on palpation firmer than normal cutaneous tissue. The two radial pulses are equal.

Roentgenologic examination of the cervical region disclosed no cervical ribs. Histologic examination confirmed the diagnosis of acrodermatitis chronica atrophicans.

DISCUSSION

DR. JOSEPH C. AMERSBACH: I cannot give much help as far as treatment is concerned. I agree with the diagnosis.

DR. J. LOWRY MILLER: The interesting feature is the unilateral characteristic. There is a history of having pain in the same side of the neck previous to the onset of the eruption. The patient received diathermy treatment for the pain. A cervical rib was thought of at the first visit to the clinic as a possible cause of the pain and subsequent eruption, but this has been ruled out by roentgenologic examination.

DR. MAURICE J. COSTELLO: It is an unusual and interesting case. For practical purposes one may say that the disease is unilateral. I believe she has begin-

ning changes on the other arm. They are faint enough, I admit, and would not have been suspected if she did not have frank lesions on the right forearm and arm.

DR. RICHARD J. KELLY: I think that the patient should be investigated carefully from the standpoint of a thyroid deficiency, and I am interested in knowing whether there is any difference in blood pressure between one upper extremity and the other. I suppose a roentgenogram of the chest has been made.

DR. ROYAL M. MONTGOMERY: The unusual feature in this case is the fact that the eruption is unilateral and limited only to the right arm. I doubt whether the severe sunburn mentioned in the history has anything to do with the causation. If the sunburn were equally distributed, both arms should be affected.

DR. GERALD F. MACHACEK: I think the suggestion of checking blood pressure in both arms is a good one. The pulse was felt in both radial arteries, and the two seemed to be equal. A roentgenologic examination disclosed no sign of a cervical rib. Once in a while instead of a cervical rib there is present a band of fascia across the brachial vessels and cervical plexus, which gives the same symptoms as a cervical rib but which cannot be felt and cannot be seen by roentgenologic examination. The patient complains of pain in the third and fourth fingers of the right hand.

A Case for Diagnosis (Rosacea; Rosacea-like Tuberculid?). Presented by DR. J. LOWRY MILLER.

J. S., aged 42, was first seen at the clinic of the New York City Hospital, in January 1945. He complained of an erythematous eruption present on his face for twenty years. He stated that it began as acne during puberty but has been present for twenty years. No treatment of any kind has been given. Aside from an operation to remove a bony spur which was causing pain in his leg and numbness in his foot, he has enjoyed good health.

Examination shows numerous pea-sized red macules and papules scattered over the entire face. One papulopustule is present. Telangiectases are seen in many of the lesions.

Roentgenograms of the bones of the legs revealed changes suggestive of Paget's disease of the bone. Histologic examination of the lesion from the forehead established a diagnosis of rosacea and showed no changes suggestive of a tuberculid.

DISCUSSION

DR. JOSEPH C. AMERSBACH: I believe this is rosacea. The lesions do not strike me as being of the Lewandowski type. I do not know how much specific therapy has been instituted or what the diet has been.

DR. MAURICE J. COSTELLO: I think that the patient has rosacea, in spite of the fact that he has had it so long. I think that it is unusual to have rosacea persist so long without remission. The man is a heavy coffee drinker. If he is asked to follow a diet for patients with rosacea and if dilute hydrochloric acid is administered the eruption should improve, but I am inclined to think that he is going to have rosacea indefinitely.

DR. RICHARD J. KELLY: I believe this is rosacea. There is a possibility that the patient may have had a juvenile acne. However, at present the characteristic features of the eruption place it in the category of rosacea. There is a definite history of ingestion of strong coffee.

DR. GERALD F. MACHACEK: My impression also is that it is probably rosacea. However, I think another biopsy should be performed on a good fleshy nodule as it is possibly a rosacea-like tuberculid. I examined one biopsy specimen, and that showed only chronic inflammatory changes. That in no way eliminates the possibility of a tuberculid.

DR. ROYAL M. MONTGOMERY: In view of the fact that he has had the rosacea so long, I suggest a course of bismuth subsalicylate. Some patients with rosacea respond to this type of therapy.

James Lowry Miller, M.D., *President*

Leslie P. Barker, M.D., *Secretary*

March 19, 1945

Subcutaneous Recurrent Effusion. Presented by DR. GERALD F. MACHACEK.

A. P., white, aged 43, presents on the outer aspect of the right thigh a diffuse swelling extending from the middle of the upper third to almost the knee. There is at present no discoloration except for a scar in the middle of the thigh where there originally was an infected lacerated wound which was superficial. On Feb. 1, 1945, the patient suffered an extensive contusion of the right thigh with laceration. There was discoloration which resulted two weeks later in subcutaneous liquefaction. On palpation, a soft boggy mass in which a fluid wave was elicited, was present. This was aspirated, and 2½ ounces (70.9 Gm.) of somewhat turbid straw-colored fluid was obtained. One week later a smaller fluctuating mass was present near the knee. One ounce (28.3 Gm.) of turbid yellow fluid was obtained on aspiration. Two days ago, there was a reaccumulation of liquid which again extended from the region of the hip to the knee. No elevation of temperature or tachycardia was present. The patient is comfortable, being merely upset by the formation of this elongated liquid-filled mass, with soft fluctuant walls.

DISCUSSION

DR. J. LOWRY MILLER: I believe that the effusion results from an inflammation of the sheath of the vastus lateralis. There is a history of injury in this area. I should suggest aspiration of the fluid and injection of 5 per cent phenol solution as a method of treatment.

DR. JOSEPH C. AMERSBACH: I feel, as Dr. Miller suggested, that it is a condition resulting from a hematoma and possibly an inflammation of the vastus lateralis and should suggest incision leaving a drain in the site of the incision for probably a week or ten days. If this does not clear up following this procedure, I believe that the injection of some sclerosing solution would be of benefit.

DR. RICHARD J. KELLY: This man had an injury and a definite traumatic hematoma. It was aspirated by Dr. Machacek, cleared and recurred. I should suggest, if it is possible, that a guinea pig be inoculated. I should like to ask the presenter whether there is any arthrosis of the knee joint.

DR. GERALD F. MACHACEK: I agree with the diagnosis of inflammation of the fascial sheath. The thing that puzzles me is whether it is or is not connected with some of the bursae of the knee, but I do not think that it is. I think that some sclerosing solution will have to be injected or some permanent drainage made.